EXHIBIT B

UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

In re: NEURONTIN MARKETING, SALES PRACTICES, AND PRODUCTS LIABILITY LITIGATION	MDL Docket No. 1629
	Master File No. 04-10981
	Judge Patti B. Saris
THIS DOCUMENT RELATES TO:	
	Magistrate Judge Leo T. Sorokin
ALL PRODUCTS LIABILITY CASES	

PLAINTIFF'S SUPPLEMENTAL EXPERT DISCLOSURE

Plaintiffs, by and through their attorneys, FINKELSTEIN & PARTNERS, LLP, pursuant to Fed. R. Civ. P. 26(a)(2) and 26(e) hereby supplement previous expert disclosure as to experts, Stefan Kruszewski, M.D., Michael Trimble, M.D., and Cheryl Blume, PhD, as it pertains to materials reviewed, considered and/or relied upon, and in providing opinion testimony that is consistent and supportive of their previously disclosed opinions in this litigation:

Patorno, E., et al., *Anticonvulsant Medication and the Risk of Suicide, Attempted Suicide, or Violent Death*, JAMA, 4/14/10 (A copy is attached hereto).

Dated: April 14, 2010

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CERTIFICATE OF SERVICE

I HEREBY CERTIFY that on this 14th day of April 2010, I caused to be served a true and correct copy of the foregoing Supplemental Expert Disclosure to:

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Anticonvulsant Medications and the Risk of Suicide, Attempted Suicide, or Violent Death

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Context In 2008, the US Food and Drug Administration mandated warning labeling for anticonvulsant medications regarding the increased risk of suicidal thoughts and behaviors. The decision was based on a meta-analysis not sufficiently large to investigate individual drugs.

Objective To evaluate the risk of suicidal acts and combined suicidal acts or violent death associated with individual anticonvulsants.

Design A cohort study of the risk of suicidal acts and combined suicidal acts or violent death in patients beginning use of anticonvulsant medications compared with patients initiating a reference anticonvulsant drug.

Setting and Patients Patients 15 years and older from the HealthCore Integrated Research Database (HIRD) who began taking an anticonvulsant between July 2001 and December 2006.

Main Outcome Measures Cox proportional hazards models and propensity score–matched analyses were used to evaluate risk of attempted or completed suicide and combined suicidal acts or violent death, controlling for psychiatric comorbidities and other risk factors, among individual anticonvulsants compared with topiramate and secondarily carbamazepine.

Results The study identified 26 completed suicides, 801 attempted suicides, and 41 violent deaths in 297 620 new episodes of treatment with an anticonvulsant (overall median follow-up, 60 days). The incidence of the composite outcomes of completed suicides, attempted suicides, and violent deaths for anticonvulsants used in at least 100 treatment episodes ranged from 6.2 per 1000 person-years for primidone to 34.3 per 1000 person-years for oxcarbazepine. The risk of suicidal acts was increased for gabapentin (hazard ratio [HR], 1.42; 95% confidence interval [CI], 1.11-1.80), lamotrigine (HR, 1.84; 95% CI, 1.43-2.37), oxcarbazepine (HR, 2.07; 95% CI, 1.52-2.80), tiagabine (HR, 2.41; 95% CI, 1.65-3.52), and valproate (HR, 1.65; 95% CI, 1.25-2.19), compared with topiramate. The analyses including violent death produced similar results. Gabapentin users had increased risk in subgroups of younger and older patients, patients with mood disorders, and patients with epilepsy or seizure when compared with carbamazepine.

Conclusion This exploratory analysis suggests that the use of gabapentin, lamotrigine, oxcarbazepine, and tiagabine, compared with the use of topiramate, may be associated with an increased risk of suicidal acts or violent deaths.

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ANTICONVULSANT MEDICATIONS are a heterogeneous pharmacologic class characterized by various chemical structures and postulated mechanisms of action. They represent the main therapeutic approach for patients with epilepsy, but labeled indications also include bipolar disorder, mania, neuralgia, migraine, and neuropathic pain.[1-3] Their off-label use is rapidly increasing as well.[4,5] The wide range of indications and common use of anticonvulsants in patients with or without psychiatric comorbidities make their safety an issue of great relevance.

In 2008 the US Food and Drug Administration (FDA) published a meta-analysis including data from 199 placebo-controlled trials of 11 anticonvulsant drugs.[6] The FDA found that patients taking anticonvulsant drugs had approximately twice the risk of suicidal behavior or ideation (0.43 per 100) compared with patients receiving placebo (0.22 per 100). Subsequently, the FDA required new labeling for all anticonvulsant medications, including a warning about the increased risk of suicidal thoughts and behavior.[7-9] Although an increased risk in these outcomes was observed in the meta-analysis, its limited size and small number of events, largely representing cases of suicidal ideation only, prevented definitive conclusions about the safety of individual agents. Furthermore, in many trials included in the meta-analysis, the anticonvulsant drugs were used as an adjunctive therapy, further complicating the assessment of their individual effect. Thus, the FDA meta-analysis could not provide patients or cli-

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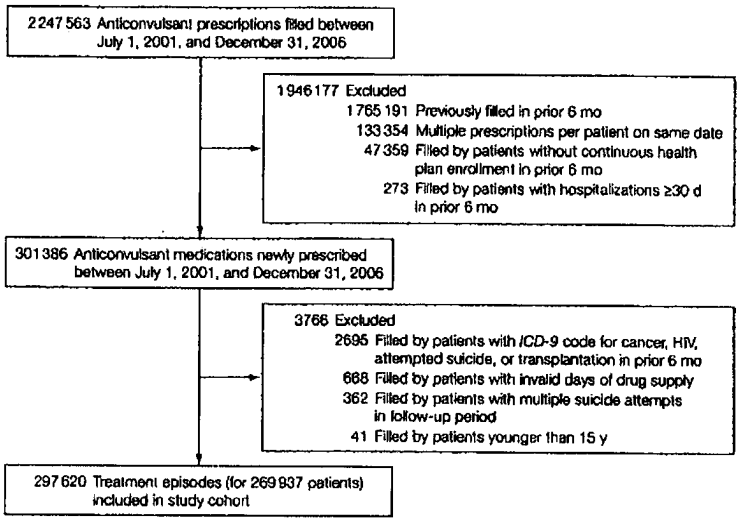
Figure 1. Flowchart of Study Cohort of Treatment Episodes



ICD-9 indicates *International Classification of Diseases, Ninth Revision*; HIV, human immunodeficiency virus.

nicians with clear guidance on risk for specific agents or patient subgroups.[10]

The objective of this study was to evaluate the increased risk of attempted or completed suicide, and combined suicidal acts or violent death, associated with a range of individual anticonvulsant agents and within patient subgroups.

METHODS

We conducted a cohort study to compare the risk of attempted or completed suicide and combined suicidal acts or violent death in patients beginning to take anticonvulsant medications with the risk in patients beginning to take a reference anticonvulsant drug (primarily topiramate and secondarily carbamazepine). The analysis was restricted to new users of the study drugs to facilitate detection of events occurring shortly after initiation and to help define the relationship between duration of use and level of risk.[11]

Data Source

Data included medical and pharmacy claims from the HealthCore Integrated Research Database (HIRD). The HIRD contains a broad spectrum of longitudinal claims data representing all filled prescriptions and clinical encounters from health plans in the southeastern, mid-Atlantic, central, and western regions of the United States. For this study, data were available from January 1, 2004, for 14 US states (Delaware, Georgia, California, Virginia, New York, Nevada, Indiana, Kentucky, Missouri, Ohio, Wisconsin, Connecticut, Maine, and New Hampshire) with 3 states (Delaware, Georgia, and California) contributing data beginning January 1, 2001. The study cohort was followed up through December 31, 2006, the latest date for which data on the exact date and cause of death from the National Death Index (NDI) were available.

Study Population

All participants aged 15 years and older who began taking an anticonvulsant drug between July 2001 through December 2006, and who had 6 months of continuous health plan enrollment preceding the drug initiation date (index date), were eligible for the study cohort. Incident use required the absence of any anticonvulsant medication in the 6 months before the index date. Participants were excluded if they had received multiple anticonvulsant drugs on the index date and if, in the 6 months before the index date, they had recorded diagnoses for attempted suicide or medical conditions that could have influenced the risk of suicidal acts, such as cancer, human immunodeficiency virus, or long hospitalization (length of stay >30 days) (FIGURE 1).

Personal identifiers were removed from the data set before the analysis to protect subject confidentiality. The study was approved by the institutional review board of Brigham and Women's Hospital and Quorum Review Inc.

Anticonvulsant Medications and Drug Exposure

The anticonvulsant medications considered included carbamazepine, ethosuximide, felbamate, gabapentin, lamotrigine, levetiracetam, oxcarbazepine, phenobarbital, phenytoin, pregabalin, primidone, tiagabine, topiramate, valproate, and zonisamide. The heterogeneous utilization pattern of anticonvulsant medications makes the choice of a common reference drug particularly challenging. Topiramate was chosen as the primary reference drug because it was the second most commonly used agent in the study population and because it is used for a wide range of indications. However, despite its broad range of uses, topiramate is not commonly used as first-line therapeutic approach in epilepsy or seizure disorder. To investigate the risk of suicidal events in patients beginning to use anticonvulsants for epilepsy, we used carbamazepine, an anticonvulsant widely used for initial treatment of epilepsy, as a reference drug in a secondary analysis.

Based on the medication prescribed on the index date, each subject was identified as beginning to take a specific anticonvulsant agent. Follow-up began on the day following the initial fill date. Participants were followed up for 180 days, until drug discontinuation or switching, the occurrence of a study outcome, death for causes not included in the study outcome, end of continuous health plan enrollment, or the end of the observation period, whichever came first. Patients could have gaps of up to 30 days between prescription fill dates in the calculation of continuous therapy. In the case of drug discontinuation or switching, the ex-

posure risk window for each patient treatment episode extended until 30 days after the expiration of the supply of the last fill. Patients could contribute more than 1 treatment episode if they had a 6-month washout period without use of any study drug. In a secondary analysis mimicking an "intention-to-treat" approach, patients were followed up from the day following the first fill for 180 days without considering drug discontinuation or switching, carrying forward exposure to the first-used drug.

Outcomes

We identified suicide attempts through emergency department (ED) visits and hospitalizations with a diagnosis of suicide and self-inflicted injury (E950.x-958.x) coded using *International Classification of Diseases, Ninth Revision (ICD-9)*[12] and recorded in medical claims in the HIRD. The use of the *ICD-9* coding system for the identification of suicide attempts has been found to have a positive predictive value of 86%.[13] In addition, a validation study of injury-related deaths found that suicides are reliably documented on death certificates with specificity and sensitivity for the individual codes for intentional self-harm all greater than 90%.[14] In the United States, *ICD-9* E-codes are incompletely forwarded from hospitals to payers.[15] To address this issue, for the identification of cases of attempted suicide, we also used an algorithm that combined specific *ICD-9* codes for injuries with other diagnoses and that was shown to have a specificity of 98% and positive predictive value of 73% in a Nationwide Inpatient Sample.[16] Participant data were censored after the first attempted suicide without considering other outcomes on subsequent treatment episodes.

After routine cross-checking of the HIRD with the US Social Security Administration Master Death Index to determine which members of the HIRD had died, we identified the exact date and cause of death for these patients from the NDI. Cases of completed suicide were identified through recorded *ICD-10* codes for intentional self-harm (X60-X84), while violent deaths were identified as S00-T78, V01-V99, W00-X59, and Y10-Y34.[17] We chose to also investigate violent deaths because mortality due to injuries or accidents accounts for a proportion of suicides,[14,18] reaching 87% among accidental deaths suspected as being suicidal.[19]

Potential Confounders and Other Variables

Patient characteristics were assessed during the 6 months preceding cohort entry, including the index date (the first fill). Demographic data (age and sex), calendar year, and comorbidities that could have been associated with a higher risk of attempted or completed suicide and violent death were investigated via *ICD-9* codes and Current Procedural Terminology 4 codes (CPT-4)[20] and medication use via National Drug Codes. These comorbidities included psychiatric disorders, such as bipolar disorder, anxiety, psychotic disorders, substance abuse, delirium, dementia, and other psychiatric disorders; and neurological disorders, such as epilepsy and seizure disorders, neuropathy and neuropathic pain, migraine, head injury, Parkinson disease, multiple sclerosis, amyotrophic lateral sclerosis, and other neurological disorders. We also identified other comorbidities as potential confounders, including myocardial infarction, cerebrovascular disease, heart failure, diabetes mellitus, chronic lung disease, renal failure, and other severe chronic disorders, and health care utilization, including previous hospitalizations, physician visits, psychiatric hospitalizations, use of psychotropic medications, and total number of medications used.

Statistical Analysis

We then defined demographic characteristics and selected coexisting clinical conditions and health care utilization measures among new users of each anticonvulsant medication considered through cross-tabulations by drug exposure. For each medication exposure on the index date, the number of participants; number of treatment episodes; length of follow-up period; and number of events and incidence rates for attempted suicide, attempted or completed suicide, and any suicidal event or violent death were calculated until drug discontinuation or switching. The primary analysis was limited to 180 days of follow-up; in a secondary analysis we extended the follow-up period to 360 days. For the 180-day follow-up analysis, the population was followed up via 2 methods: until drug discontinuation or switching (primary as-treated analysis) and carrying forward the first drug exposure until day 180 (secondary cumulative analysis). The number of participants lost to 180 days of follow-up, excluding the number of participants who developed any suicidal event or violent death, was 245 398 in the primary as-treated analysis and 88 849 in the secondary cumulative analysis. These patients were censored at the time they were lost to follow-up.

To control for potential differences among new users of anticonvulsant medications, multivariate-adjusted Cox proportional hazards models were used as well as high-dimensional propensity score analysis.[21] A 2-sided statistical significance level of .05 was applied.

We fitted unadjusted; age-, sex-, and calendar year–adjusted; and multivariate-adjusted (for all the variables previously mentioned) Cox proportional hazards models to evaluate all outcomes in 180 days among users of all anticonvulsant medications compared with new users of topiramate until discontinuation or switching of the study drug.

To improve covariate adjustment, we used high-dimensional propensity score estimation. Initiation of each anticonvulsant medication was modeled pairwise against topiramate initiation, the common reference group, and then propensity score–matched using the greedy matching algorithm,[22] which has been shown to perform well in balancing 2 comparison groups.[23] Because pregabalin was not on the market before 2005, new users of pregabalin were propensity score–matched with topiramate beginning January 2005. Rate ratios (RRs) and rate differences (RDs) with 95% confidence intervals (CIs) for all outcomes

were calculated, and adjusted Kaplan-Meier curves were plotted among selected matched groups. Forest plots of the RRs for attempted or completed suicide were produced for subgroups defined by age (15-24 and 25-64 years), recorded diagnosis of mood disorders or its therapy (antidepressant medications or lithium), and recorded diagnosis of epilepsy or seizure disorders.

Adjustments for multiple comparisons were not considered. In this exploratory analysis, we limited analyses to estimation of effects and precision rather than any formal statistical testing.[24,25] Statistical analyses were performed using SAS versions 9.1 and 9.2 (SAS Institute, Cary, North Carolina).

RESULTS

We identified 297 620 new treatment episodes of anticonvulsant medications (Figure 1), among which 57 853 were represented by topiramate. The most frequently prescribed medications were gabapentin (48.0%), topiramate (19.4%), lamotrigine (7.5%), and valproate (6.2%). TABLE 1, TABLE 2, and eTable 1 (available at http://www.jama.com) show variations in patient characteristics among study drugs that are consistent with the wide spectrum of uses of anticonvulsant drugs. Patients beginning to take topiramate were more likely than patients beginning to take other anticonvulsant medications to be female, to have had a diagnosis of migraine or headache, to have had an ambulatory visit, and to have used antimigraine medications in the 6 months prior to drug initiation. New users of topiramate also had a lower proportion of epilepsy or seizure disorders and previous hospitalizations in the period preceding the drug initiation. The new users of other anticonvulsants were more likely to have had diagnoses of epilepsy or seizure disorder (levetiracetam and phenytoin), neuropathic pain (carbamazepine, gabapentin, and pregabalin), depressive disorder, manic-depressive disorder, or anxiety (lamotrigine, oxcarbazepine, valproate, and tiagabine) and to have used antidepressant (lamotrigine and tiagabine), antipsychotic (lamotrigine and valproate), and analgesic medications (gabapentin, pregabalin, and tiagabine).

The overall mean (SD) follow-up for anticonvulsant medications was 91 (52) days and the median was 60 days (interquartile range, 60-125 days). The mean follow-up time for topiramate treatment was 97 days and the median was 60 days (TABLE 3). Patients beginning to take lamotrigine had the longest time receiving therapy, with mean and median follow-up periods of 109 and 98 days, respectively. Phenobarbital and pregabalin treatment episodes had the shortest

Table 1. Selected Patient Characteristics by Drug Exposure (New Treatment Episodes) for 7 of 13 Anticonvulsant Medications[a]

	No. (%)						
	Topiramate	Carbamazepine	Gabapentin	Lamotrigine	Levetiracetam	Oxcarbazepine	Phenobarbital
Observations	57 853 (19.4)	9859 (3.3)	142 865 (48.0)	22 256 (7.5)	3975 (1.3)	8579 (2.9)	2130 (0.7)
Demographics							
Female	47 803 (82.6)	5851 (59.3)	86 846 (60.8)	14 327 (64.4)	2433 (61.2)	5048 (58.8)	1288 (60.5)
Age, mean (SD), y	41 (13)	46 (17)	51 (14)	38 (14)	46 (17)	37 (16)	47 (16)
Median, y	41	46	51	38	46	37	45
Health services utilization							
No. of medications, mean (SD)	8 (6)	6 (6)	9 (6)	7 (6)	7 (7)	7 (6)	7 (7)
Median, No.	7	5	8	6	6	5	5
Hospitalization	4988 (8.6)	1375 (13.9)	22 764 (15.9)	2746 (12.3)	1160 (29.2)	1542 (18.0)	520 (24.4)
Ambulatory visits	47 486 (82.1)	6807 (69.0)	110 696 (77.5)	15 775 (70.9)	3139 (79.0)	6259 (73.0)	1445 (67.8)
Hospitalization for any psychiatric disorder	1984 (3.4)	638 (6.5)	6242 (4.4)	1986 (8.9)	397 (10.0)	1007 (11.7)	266 (12.5)
Neurological and psychiatric comorbidities							
Epilepsy	618 (1.1)	704 (7.1)	386 (0.3)	741 (3.3)	773 (19.4)	523 (6.1)	123 (5.8)
Convulsions	1041 (1.8)	1174 (11.9)	920 (0.6)	926 (4.2)	1289 (32.4)	845 (9.8)	215 (10.1)
Neuropathic pain	1383 (2.4)	1617 (16.4)	23 202 (16.2)	939 (4.2)	362 (9.1)	795 (9.3)	116 (5.4)
Migraine	21 293 (36.8)	444 (4.5)	6159 (4.3)	990 (4.4)	596 (15.0)	398 (4.6)	120 (5.6)
Depressive disorder	9773 (16.9)	1238 (12.6)	15 374 (10.8)	8963 (40.3)	462 (11.6)	2648 (30.9)	265 (12.4)
Manic depressive disorder	2426 (4.2)	692 (7.0)	2081 (1.5)	6586 (29.6)	62 (1.6)	1843 (21.5)	30 (1.4)
Psychosis	516 (0.9)	180 (1.8)	961 (0.7)	634 (2.8)	121 (3.0)	344 (4.0)	30 (1.4)
Alcohol and drug abuse or dependence	2195 (3.8)	604 (6.1)	6992 (4.9)	1615 (7.3)	279 (7.0)	851 (9.9)	363 (17.0)
Delirium	183 (0.3)	81 (0.8)	594 (0.4)	149 (0.7)	75 (1.9)	87 (1.0)	26 (1.2)
Dementia	239 (0.4)	144 (1.5)	1261 (0.9)	135 (0.6)	187 (4.7)	122 (1.4)	28 (1.3)
Other psychiatric disorders	4709 (8.1)	608 (6.2)	6477 (4.5)	3145 (14.1)	306 (7.7)	1385 (16.1)	105 (4.9)
Use of other psychotropic medications							
Antidepressants	29 963 (51.8)	3211 (32.6)	55 194 (38.6)	15 266 (68.6)	1592 (40.1)	4803 (56.0)	647 (30.4)
Lithium	823 (1.4)	242 (2.5)	768 (0.5)	2054 (9.2)	34 (0.9)	405 (4.7)	11 (0.5)
Antipsychotics	4725 (8.2)	956 (9.7)	6103 (4.3)	5669 (25.5)	273 (6.9)	1806 (21.1)	138 (6.5)
Analgesics	28 319 (48.9)	4145 (42.0)	94 639 (66.2)	6867 (30.9)	1837 (46.2)	3059 (35.7)	924 (43.4)

[a] Six months prior to index date.

Table 2. Selected Patient Characteristics by Drug Exposure (New Treatment Episodes) for 6 of 13 Anticonvulsant Medications[a]

	No. (%)					
	Phenytoin	Pregabalin	Primidone	Tiagabine	Valproate	Zonisamide
Observations	10 531 (3.5)	9086 (3.1)	3104 (1.0)	5497 (1.9)	18 295 (6.2)	3528 (1.2)
Demographics						
Female	4640 (44.1)	5419 (59.6)	1567 (50.5)	3320 (60.4)	10 118 (55.3)	2608 (73.9)
Age, mean (SD), y	48 (18)	56 (15)	59 (16)	44 (13)	41 (18)	43 (14)
Median, y	48	55	60	44	39	43
Health services utilization						
No. of medications, mean (SD)	6 (6)	10 (7)	8 (7)	9 (7)	7 (6)	7 (7)
Median, No.	4	9	7	8	6	6
Hospitalization	4657 (44.2)	1311 (14.4)	377 (12.1)	734 (13.4)	4045 (22.1)	388 (11.0)
Ambulatory visits	6230 (59.2)	6135 (67.5)	2477 (79.8)	4526 (82.3)	11 876 (64.9)	2999 (85.0)
Hospitalization for any psychiatric disorder	1597 (15.2)	253 (2.8)	89 (2.9)	394 (7.2)	2903 (15.9)	128 (3.6)
Neurological and psychiatric comorbidities						
Epilepsy	1717 (16.3)	34 (0.4)	33 (1.1)	27 (0.5)	601 (3.3)	164 (4.6)
Convulsions	5141 (48.8)	61 (0.7)	62 (2.0)	65 (1.2)	1152 (6.3)	206 (5.8)
Neuropathic pain	169 (1.6)	1154 (12.7)	105 (3.4)	312 (5.7)	227 (1.2)	174 (4.9)
Migraine	360 (3.4)	347 (3.8)	70 (2.3)	364 (6.6)	2169 (11.9)	884 (25.1)
Depressive disorder	808 (7.7)	751 (8.3)	254 (8.2)	1588 (28.9)	5096 (27.9)	567 (16.1)
Manic depressive disorder	74 (0.7)	83 (0.9)	36 (1.2)	291 (5.3)	4259 (23.3)	140 (4.0)
Psychosis	327 (3.1)	39 (0.4)	27 (0.9)	81 (1.5)	1349 (7.4)	24 (0.7)
Alcohol and drug abuse or dependence	1121 (10.6)	292 (3.2)	85 (2.7)	519 (9.4)	1776 (9.7)	144 (4.1)
Delirium	248 (2.4)	36 (0.4)	11 (0.4)	45 (0.8)	328 (1.8)	21 (0.6)
Dementia	566 (5.4)	63 (0.7)	106 (3.4)	35 (0.6)	925 (5.1)	29 (0.8)
Other psychiatric disorders	544 (5.2)	314 (3.5)	86 (2.8)	630 (11.5)	2535 (13.9)	298 (8.4)
Use of other psychotropic medications						
Antidepressants	2279 (21.6)	3840 (42.3)	1030 (33.2)	3666 (66.7)	10 130 (55.4)	1795 (50.9)
Lithium	20 (0.2)	35 (0.4)	33 (1.1)	97 (1.8)	867 (4.7)	48 (1.4)
Antipsychotics	531 (5.0)	439 (4.8)	116 (3.7)	752 (13.7)	4601 (25.1)	262 (7.4)
Analgesics	4172 (39.6)	6575 (72.4)	1153 (37.1)	3307 (60.2)	6647 (36.3)	1921 (54.5)

[a]Six months prior to index date.

Table 3. Study Population, Follow-up, and Event Rates

			Follow-up, d		Events Within 180 d, No. (Incidence Rate per 1000 Person-Years)[a]			
	Participants, No.	Treatment Episodes, No.	Mean (SD)	Median (IQR)	Attempted Suicide (n = 801)	Completed Suicide (n = 26)	Attempted or Completed Suicide (n = 827)	Attempted or Completed Suicide or Violent Death (n = 868)
Topiramate[b]	52 127	57 853	97 (54)	60 (60-152)	109 (7.1)	2 (0.1)	111 (7.2)	115 (7.4)
Carbamazepine	8778	9859	87 (51)	60 (60-120)	20 (8.6)	1 (0.4)	21 (9.0)	21 (9.0)
Ethosuximide	42	47	77 (45)	60 (60-60)	0	0	0	0
Felbamate	13	15	101 (63)	66 (60-181)	0	0	0	0
Gabapentin	130 698	142 865	85 (49)	60 (60-111)	228 (6.9)	8 (0.2)	235 (7.1)	250 (7.5)
Lamotrigine	20 062	22 256	109 (58)	98 (60-181)	174 (26.1)	7 (1.0)	181 (27.1)	186 (27.9)
Levetiracetam	3544	3975	95 (54)	60 (60-146)	10 (9.7)	0	10 (9.7)	11 (10.7)
Oxcarbazepine	7725	8579	98 (54)	67 (60-154)	75 (32.6)	1 (0.4)	76 (33.0)	79 (34.3)
Phenobarbital	1859	2130	73 (50)	60 (37-90)	4 (9.4)	0	4 (9.4)	4 (9.4)
Phenytoin	9833	10 531	98 (56)	66 (60-164)	18 (6.4)	1 (0.4)	19 (6.7)	20 (7.1)
Pregabalin	7875	9086	76 (46)	60 (50-97)	9 (4.7)	0	9 (4.7)	12 (6.3)
Primidone	2871	3104	95 (54)	60 (60-150)	2 (2.5)	1 (1.2)	3 (3.7)	5 (6.2)
Tiagabine	4853	5497	88 (49)	60 (60-120)	38 (28.7)	0	38 (28.7)	39 (29.5)
Valproate	16 692	18 295	92 (52)	60 (60-127)	107 (23.2)	5 (1.1)	112 (24.3)	118 (25.6)
Zonisamide	2965	3528	90 (50)	60 (60-120)	7 (8.0)	0	7 (8.0)	8 (9.2)

Abbreviation: IQR, interquartile range.
[a]As-treated analysis censoring at termination of health plan eligibility, treatment discontinuation, drug switching, event, or 180 days, whichever came first.
[b]Reference drug.

therapy time. There were 827 attempted or completed suicides and a total of 868 combined events inclusive of attempted or completed suicides or violent deaths within 180 days after the initiation of any anticonvulsant medication.

The risk of attempted suicide, attempted or completed suicide, and any suicidal event or violent death within 180 days among other anticonvulsant new treatment episodes compared with topiramate is shown in TABLE 4. Results of the multivariate-adjusted Cox regression analysis indicated that the risk for all outcomes was increased for gabapentin, lamotrigine, oxcarbazepine, tiagabine, and valproate new treatment use compared with topiramate use. In particular, the risk of attempted or completed suicide was meaningfully increased for gabapentin (hazard ratio [HR], 1.42; 95% CI, 1.11-1.80), lamotrigine (HR, 1.84; 95% CI, 1.43-2.37), oxcarbazepine (HR, 2.07; 95% CI, 1.52-2.80), tiagabine (HR, 2.41; 95% CI, 1.65-3.52), and valproate (HR, 1.65; 95% CI, 1.25-2.19). Similar results were obtained in the analysis evaluating any suicidal event or violent death. The first exposure within the exposure carried-forward 180 days analysis, which is less subject to potential bias due to informative switching or discontinuation, produced similar results (eTable 2). Extending the study period to 360 days of follow-up (eTable 3 and eTable 4) after drug initiation yielded no substantive differences from the 180-day analysis.

A secondary analysis using high-dimension propensity score matching confirmed the findings of the analysis for gabapentin, oxcarbazepine, and tiagabine treatment compared with topiramate episodes with regard to attempted or completed suicide and combined suicidal acts or violent death (eTables 5, 6, and 7). In particular, the risk of attempted or completed suicide was increased for gabapentin (RR, 1.99; 95% CI, 1.45-2.73; RD, 5.59 per 1000 person-years; 95% CI, 3.01-8.17 per 1000 person-years), oxcarbamazepine (RR, 1.49; 95% CI, 1.01-2.20; RD, 10.00 per 1000 person-years; 95% CI, 0.35-19.65 per 1000 person-years), and tiagabine (RR, 1.98; 95% CI, 1.15-3.41; RD, 14.06; 95% CI, 2.97-25.15 per 1000 person-years) (eTable 6).

In the high-dimension propensity score analysis, lamotrigine treatment episodes had a higher risk than topiramate for suicidal events. New treatment with

Table 4. Hazard Ratios of Study Outcomes Within 180 Days[a]

	HR (95% CI)		
	Suicide Attempt	Attempted or Completed Suicide	Attempted or Completed Suicide or Violent Death
Unadjusted analysis			
Carbamazepine	1.18 (0.73-1.90)	1.22 (0.76-1.94)	1.18 (0.74-1.87)
Gabapentin	0.94 (0.75-1.18)	0.95 (0.76-1.19)	0.98 (0.79-1.22)
Lamotrigine	3.81 (3.00-4.85)	3.90 (3.08-4.94)	3.86 (3.06-4.87)
Levetiracetam	1.37 (0.72-2.62)	1.34 (0.70-2.57)	1.43 (0.77-2.65)
Oxcarbazepine	4.62 (3.45-6.20)	4.60 (3.44-6.16)	4.61 (3.47-6.14)
Phenobarbital	1.26 (0.47-3.43)	1.24 (0.46-3.36)	1.20 (0.44-3.26)
Phenytoin	0.91 (0.55-1.50)	0.94 (0.58-1.53)	0.96 (0.60-1.54)
Pregabalin	0.64 (0.32-1.26)	0.63 (0.32-1.24)	0.81 (0.45-1.47)
Primidone	0.35 (0.09-1.41)	0.51 (0.16-1.61)	0.83 (0.34-2.02)
Tiagabine	3.96 (2.73-5.72)	3.88 (2.69-5.61)	3.85 (2.68-5.54)
Valproate	3.25 (2.49-4.24)	3.33 (2.56-4.34)	3.39 (2.63-4.39)
Zonisamide	1.11 (0.52-2.39)	1.09 (0.51-2.34)	1.21 (0.59-2.47)
Age-, sex-, and calendar year–adjusted analysis			
Carbamazepine	1.38 (0.85-2.22)	1.38 (0.87-2.21)	1.32 (0.83-2.11)
Gabapentin	1.52 (1.20-1.92)	1.48 (1.17-1.87)	1.49 (1.18-1.87)
Lamotrigine	3.51 (2.76-4.48)	3.58 (2.82-4.56)	3.56 (2.81-4.50)
Levetiracetam	1.63 (0.85-3.12)	1.57 (0.82-3.01)	1.65 (0.89-3.06)
Oxcarbazepine	3.94 (2.92-5.32)	3.88 (2.88-5.22)	3.90 (2.92-5.22)
Phenobarbital	1.61 (0.59-4.37)	1.54 (0.57-4.17)	1.46 (0.54-3.96)
Phenytoin	1.24 (0.75-2.05)	1.23 (0.75-2.01)	1.22 (0.76-1.97)
Pregabalin	1.37 (0.69-2.73)	1.30 (0.65-2.59)	1.59 (0.87-2.92)
Primidone	0.78 (0.19-3.16)	1.08 (0.34-3.42)	1.62 (0.66-3.99)
Tiagabine	4.58 (3.15-6.66)	4.38 (3.02-6.36)	4.30 (2.98-6.22)
Valproate	3.10 (2.35-4.08)	3.11 (2.37-4.07)	3.15 (2.42-4.10)
Zonisamide	1.19 (0.56-2.56)	1.16 (0.54-2.50)	1.28 (0.63-2.62)
Adjusted analysis[b]			
Carbamazepine	1.23 (0.76-2.00)	1.24 (0.77-1.99)	1.19 (0.74-1.91)
Gabapentin	1.44 (1.13-1.83)	1.42 (1.11-1.80)	1.42 (1.12-1.80)
Lamotrigine	1.79 (1.38-2.31)	1.84 (1.43-2.37)	1.86 (1.45-2.39)
Levetiracetam	1.71 (0.88-3.31)	1.63 (0.84-3.16)	1.66 (0.88-3.14)
Oxcarbazepine	2.09 (1.54-2.85)	2.07 (1.52-2.80)	2.12 (1.57-2.86)
Phenobarbital	1.05 (0.38-2.88)	0.99 (0.36-2.72)	0.96 (0.35-2.63)
Phenytoin	1.26 (0.72-2.20)	1.25 (0.73-2.15)	1.19 (0.70-2.02)
Pregabalin	1.22 (0.61-2.45)	1.18 (0.59-2.37)	1.44 (0.78-2.67)
Primidone	0.83 (0.20-3.47)	1.15 (0.35-3.78)	1.84 (0.71-4.72)
Tiagabine	2.49 (1.70-3.64)	2.41 (1.65-3.52)	2.40 (1.65-3.49)
Valproate	1.65 (1.25-2.20)	1.65 (1.25-2.19)	1.69 (1.29-2.23)
Zonisamide	1.28 (0.60-2.75)	1.25 (0.58-2.69)	1.37 (0.67-2.81)

Abbreviations: CI, confidence interval; HR, hazard ratio.

[a] As-treated analysis censoring at termination of health plan eligibility, treatment discontinuation, drug switching, event, or 180 days, whichever came first. Reference is topiramate.

[b] Hazard ratios were adjusted in a Cox proportional hazard regression for age, sex, calendar year, initiation of anticonvulsant medication, depression, manic disorder, psychotic disorder, anxiety, alcohol abuse or dependence, drug abuse or dependence, delirium, dementia, personality disorder, sleep disorder, other psychiatric disorder, epilepsy, seizure disorder, neuropathy and neuropathic pain, migraine, tremor, multiple sclerosis, head injury, Parkinson disease, amyotrophic lateral sclerosis, number of medications, previous hospitalization, previous ambulatory visit, previous hospitalization for epilepsy or seizure disorder, previous hospitalization for mood disorder, previous hospitalization for any psychiatric disorder, antidepressants, lithium, antipsychotics, anxiolytics, analgesics, migraine medications, hypnotics, other psychotropic medications, myocardial infarction or revascularization procedure, cerebrovascular disease, other cardiovascular disease, diabetes mellitus, chronic lung disease, hypothyroidism, osteoarthritis or rheumatoid arthritis, gastrointestinal hemorrhage and inflammatory disease, liver cirrhosis and chronic disease, renal failure and other renal disease, and blood disorder.

valproate was no longer associated with a higher rate for suicidal events.

Kaplan-Meier curves comparing the time to attempted or completed suicide within 180 days showed increased risk for suicidal events beginning within the first 30 days after treatment initiation for gabapentin (HR, 1.68; 95% CI, 1.12-2.52), lamotrigine (HR, 2.45; 95% CI, 1.60-3.76), oxcarbazepine (HR, 2.79; 95% CI, 1.70-4.55), and tiagabine (HR, 3.57; 95% CI, 2.02-6.33) new treatment episodes (FIGURE 2) (eTable 8).

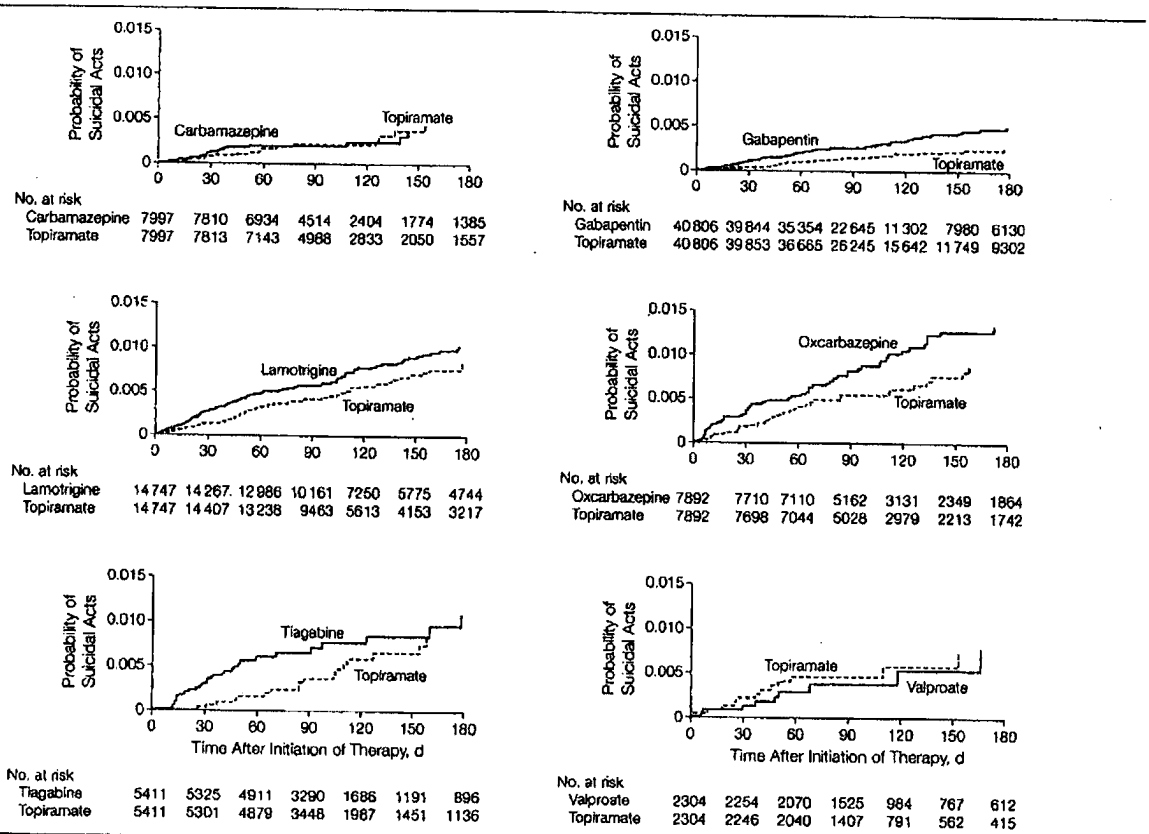
Gabapentin treatment was significantly associated with higher risk of suicidal events and combined suicidal acts or violent deaths in adults and young adults (eFigure, available at http://www.jama.com), while gabapentin, lamotrigine, oxcarbazepine, and tiagabine were associated with higher risk among adults. Gabapentin, oxcarbazepine, and tiagabine were associated with increased risk among patients with mood disorder. A subgroup of patients with a recorded diagnosis of epilepsy or seizure disorders did not produce interpretable estimates because of the scarcity of events in the propensity score–matched analysis with topiramate as the reference drug.

The propensity score–matched analysis with carbamazepine as the reference drug produced results qualitatively consistent with these findings, confirming an increased risk of suicidal events for patients beginning to take gabapentin, lamotrigine, oxcarbazepine, and tiagabine (eTable 9). In particular, we found a meaningful association between gabapentin and suicidality risk within 180 days among patients with recorded diagnosis of epilepsy or seizure disorders (RR, 13.92; 95% CI, 1.82-106.38) (eTable 10).

COMMENT

In a cohort analysis that evaluated 827 suicidal acts (801 attempted suicides and 26 completed suicides) and an additional 41 violent deaths (868 combined suicidal acts or violent deaths) in 297 620 new treatment episodes of anticonvulsant medications, we found an increased risk for these events in new users of gabapentin, lamotrigine, oxcarbazepine, and tiagabine compared with topiramate. A secondary analysis confirmed the increased risk and identified an excess of 5.6 cases of attempted or completed suicide per 1000 person-years among new users of gabapentin, 10.0 cases per 1000 person-

Figure 2. Adjusted Kaplan-Meier Plots for Time to Attempted or Completed Suicide After the Initiation of Selected Anticonvulsant Medications



High-dimension propensity score matching was used for adjustment. The primary as-treated analysis censored patient data at medication discontinuation or switching or at 180 days, whichever came first. "Suicidal acts" refers to attempted or completed suicides.

years among new users of oxcarbazepine, and 14.1 cases per 1000 person-years among new users of tiagabine compared with topiramate. The risk remained increased for gabapentin in subgroups of younger and older patients, patients with mood disorder, and patients with epilepsy or seizure disorders, although there were few events in the last group.

These findings are compatible with the results of the FDA meta-analysis, which found similarly increased risks of suicidal behavior or ideation for all anticonvulsant drugs compared with placebo, although its small numbers made it difficult to quantify these specific risks with confidence. No prior studies have directly evaluated the relationship between different anticonvulsant medications and risk of suicide in routine care. The few investigations addressing the issue were generally limited to patients with bipolar disorder, estimating the suicidal risk for anticonvulsant medications compared with lithium.[26-28] In particular, a study of 12 652 Medicaid patients diagnosed with bipolar disorder found a meaningfully increased risk for completed suicide (HR, 2.6) among gabapentin users compared with lithium users.[28] However, the number of suicides identified was limited, and risk estimates were imprecise.

Anticonvulsant medications can have psychotropic effects, including mood and behavior changes.[29-32] However, there is no clear understanding of a possible mechanism of action that could lead to suicidal behavior in patients taking these medications; the existing theories are not consistent and often derive from small trials generally performed against placebo in populations mainly including epileptic patients.[32-35] Gabapentin and lamotrigine, although they can have anxiolytic and mood stabilizer properties, have also been associated with behavioral problems such as aggression and hyperactivity, particularly in children and adults with learning disabilities and cognitive impairment.[36-40] Tiagabine has been found to produce nervousness and depressive mood in placebo-controlled trials,[41,42] potentially leading to increased risk for suicidality.[35] Few data are available on the psychotropic effects of oxcarbazepine, but a stimulant effect on psychomotor functioning compared with placebo has been observed.[43]

Anticonvulsant therapy is usually started at low dosages and increased according to the patient response, often requiring a few weeks to reach the average target dose.[44,45] We found increased risk for suicidal acts beginning within the first 14 days after treatment initiation, opening the possibility that anticonvulsant medications could induce behavioral effects prior to the achievement of their full therapeutic effectiveness.

Although we used multiple approaches in the design and analysis of the study, including a new user design, multivariate-adjusted Cox proportional hazards models, and a high-dimension propensity score–matched analysis, residual confounding by indication is still a factor to consider. Patients beginning to take lamotrigine, oxcarbazepine, and tiagabine at baseline had a higher proportion of diagnosis and treatment for depressive and manic depressive disorders than the reference group. If the presence or the severity of such clinical conditions were incompletely controlled for, this could lead to residual confounding. This pattern was not identifiable for gabapentin; its users had a higher proportion of neuropathic pain and use of pain medications. Pain could also play an important role in the process leading to suicidal behavior. The analysis with carbamazepine as a reference drug confirmed an increased risk of suicidal acts for gabapentin, with a meaningful association among patients with a diagnosis of epilepsy or seizure disorders.

The coding for suicides and suicide attempts, critical for the definition of the study outcomes, may be subject to some misclassification. If this misclassification would be nondifferential, it would result in a bias towards the null. Anticonvulsant drug switching might be related to the effect on mood of the previous anticonvulsant medication. This could make switching a predictor for suicidal acts that would not be observed in an as-treated analysis, therefore introducing bias toward the null. To minimize this potential bias, we additionally carried the first exposure forward similar to an intention-to-treat analysis without considering either drug discontinuation or switching. The results of this analysis were quite similar.

A final study limitation is the exploratory nature of this investigation. The fact that no previous studies have directly evaluated the relationship between different anticonvulsant medications and risk of suicide in routine care, the large sample size used, and the access to detailed patient information make this investigation valuable to clinical practice.

This exploratory analysis contributes to the understanding of the complex and little-understood relationship between anticonvulsant medication use and suicide risk. It suggests that the use of gabapentin, lamotrigine, oxcarbazepine, and tiagabine, compared with the use of topiramate or carbamazepine, may be associated with an increased risk of suicidal acts and combined suicidal acts or violent deaths.

Author Contributions: Dr Patorno had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Patorno, Bohn, Wahl, Avorn, Patrick, Schneeweiss.
Acquisition of data: Patorno, Bohn, Wahl, Avorn, Schneeweiss.
Analysis and interpretation of data: Patorno, Bohn, Wahl, Liu, Schneeweiss.
Drafting of the manuscript: Patorno, Schneeweiss.
Critical revision of the manuscript for important intellectual content: Patorno, Bohn, Wahl, Avorn, Patrick, Liu, Schneeweiss.
Statistical analysis: Patorno, Bohn, Wahl, Patrick, Liu, Schneeweiss.
Obtained funding: Bohn, Avorn, Schneeweiss.
Administrative, technical, or material support: Bohn, Schneeweiss.
Study supervision: Bohn, Schneeweiss.
Financial Disclosures: Dr Bohn and Mr Wahl reported being employed by HealthCore Inc, a subsidiary of WellPoint, through the study execution. Dr Bohn reported that she has recently left the company and works as an independent consultant. Dr Schneeweiss reported being a paid member of the scientific safety advisory boards of HealthCore Inc and ii4sm; being a paid consultant to HealthCore, World Health Information Science Consultants, and RTI International; and having received an investigator-initiated research grant on the safety of nonsteroidal anti-inflammatory drugs from Pfizer. No other disclosures were reported.
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Online-Only Material: eTables 1 through 10 and an eFigure are available at http://www.jama.com.

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Supplementary Online Content

Patorno E, Bohn RL, Wahl PM, et al. Anticonvulsant medications and the risk of suicide, attempted suicide, or violent death. *JAMA*. 2010;303(14):1401-1409.

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Patient characteristics by drug exposure (new treatment episodes)*

	Topiramate	Carbamazepine	Gabapentin	Lamotrigine	Levetiracetam	Oxcarbazepine	Phenobarbital	Phenytoin	Pregabalin	Primidone	Tiagabine	Valproate	Zonisamide
N of observations	57853	9859	142865	22256	3975	8579	2130	10531	9086	3104	5497	18295	3528
%	(19.4)	(3.3)	(48.0)	(7.5)	(1.3)	(2.9)	(0.7)	(3.5)	(3.1)	(1.0)	(1.9)	(6.2)	(1.2)
Demographics													
Female	47803	5851	86846	14327	2433	5048	1288	4640	5419	1567	3320	10118	2608
(%)	(82.6)	(59.3)	(60.8)	(64.4)	(61.2)	(58.8)	(60.5)	(44.1)	(59.6)	(50.5)	(60.4)	(55.3)	(73.9)
Age [Mean (SD)]	41 (13)	46 (17)	51 (14)	38 (14)	46 (17)	37 (16)	47 (16)	48 (18)	56 (15)	59 (16)	44 (13)	41 (18)	43 (14)
Median	41	46	51	38	46	37	45	48	55	60	44	39	43
Health Services Utilization													
Number of medications [Mean (SD)]	8 (6)	6 (6)	9 (6)	7 (6)	7 (7)	7 (6)	7 (7)	6 (6)	10 (7)	8 (7)	9 (7)	7 (6)	7 (7)
Median	7	5	8	6	6	5	5	4	9	7	8	6	6
Hospitalization	4988	1375	22764	2746	1160	1542	520	4657	1311	377	734	4045	388
(%)	(8.6)	(13.9)	(15.9)	(12.3)	(29.2)	(18.0)	(24.4)	(44.2)	(14.4)	(12.1)	(13.4)	(22.1)	11.0)
Ambulatory visits	47486	6807	110696	15775	3139	6259	1445	6230	6135	2477	4526	11876	2999
(%)	(82.1)	(69.0)	(77.5)	(70.9)	(79.0)	(73.0)	(67.8)	(59.2)	(67.5)	(79.8)	(82.3)	(64.9)	(85.0)
Hospitalization for epilepsy or seizure disorders	251	329	393	201	614	261	78	2438	28	11	18	429	50
(%)	(0.4)	(3.3)	(0.3)	(0.9)	(15.4)	(3.0)	(3.7)	(23.2)	(0.3)	(0.4)	(0.3)	(2.3)	(1.4)
Hospitalization for any psychiatric disorder	1984	638	6242	1986	397	1007	266	1597	253	89	394	2903	128
(%)	(3.4)	(6.5)	(4.4)	(8.9)	(10.0)	(11.7)	(12.5)	(15.2)	(2.8)	(2.9)	(7.2)	(15.9)	(3.6)
Hospitalization for mood disorder	1256	371	2626	1676	104	770	101	276	90	26	249	2080	60
(%)	(2.2)	(3.8)	(1.8)	(7.5)	(2.6)	(9.0)	(4.7)	(2.6)	(1.0)	(0.8)	(4.5)	(11.4)	(1.7)

eTable 1. Patient characteristics by drug exposure (new treatment episodes) (continued)

	Topiramate	Carbamazepine	Gabapentin	Lamotrigine	Levetiracetam	Oxcarbazepine	Phenobarbital	Phenytoin	Pregabalin	Primidone	Tiagabine	Valproate	Zonisamide
Neurological and Psychiatric Comorbidities													
Epilepsy	618	704	386	741	773	523	123	1717	34	33	27	601	164
(%)	(1.1)	(7.1)	(0.3)	(3.3)	(19.4)	(6.1)	(5.8)	(16.3)	(0.4)	(1.1)	(0.5)	(3.3)	(4.6)
Convulsions	1041	1174	920	926	1289	845	215	5141	61	62	65	1152	206
(%)	(1.8)	(11.9)	(0.6)	(4.2)	(32.4)	(9.8)	(10.1)	(48.8)	(0.7)	(2.0)	(1.2)	(6.3)	(5.8)
Neuropathic pain	1383	1617	23202	939	362	795	116	169	1154	105	312	227	174
(%)	(2.4)	(16.4)	(16.2)	(4.2)	(9.1)	(9.3)	(5.4)	(1.6)	(12.7)	(3.4)	(5.7)	(1.2)	(4.9)
Migraine	21293	444	6159	990	596	398	120	360	347	70	364	2169	884
(%)	(36.8)	(4.5)	(4.3)	(4.4)	(15.0)	(4.6)	(5.6)	(3.4)	(3.8)	(2.3)	(6.6)	(11.9)	(25.1)
Headache	15558	1389	12143	1452	766	865	174	1654	639	205	505	2327	714
(%)	(26.9)	(14.1)	(8.5)	(6.5)	(19.3)	(10.1)	(8.2)	(15.7)	(7.0)	(6.6)	(9.2)	(12.7)	(20.2)
Tremor	624	118	1173	173	131	98	23	197	72	1605	47	205	29
(%)	(1.1)	(1.2)	(0.8)	(0.8)	(3.3)	(1.1)	(1.1)	(1.9)	(0.8)	(51.7)	(0.9)	(1.1)	(0.8)
Multiple sclerosis	404	200	1961	82	70	122	6	71	140	31	52	84	37
(%)	(0.7)	(2.0)	(1.4)	(0.4)	(1.8)	(1.4)	(0.3)	(0.7)	(1.5)	(1.0)	(0.9)	(0.5)	(1.0)
Head injury	326	107	1009	185	116	111	22	607	50	16	44	275	30
(%)	(0.6)	(1.1)	(0.7)	(0.8)	(2.9)	(1.3)	(1.0)	(5.8)	(0.6)	(0.5)	(0.8)	(1.5)	(0.9)
Parkinson disease	43	25	545	35	39	15	3	52	38	130	10	106	7
(%)	(0.1)	(0.3)	(0.4)	(0.2)	(1.0)	(0.2)	(0.1)	(0.5)	(0.4)	(4.2)	(0.2)	(0.6)	(0.2)
Amyotrophic lateral sclerosis	5	1	56	1	1	5	1	4	4	1	0	1	1
(%)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.1)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)
Depressive disorder	9773	1238	15374	8963	462	2648	265	808	751	254	1588	5096	567
(%)	(16.9)	(12.6)	(10.8)	(40.3)	(11.6)	(30.9)	(12.4)	(7.7)	(8.3)	(8.2)	(28.9)	(27.9)	(16.1)
Manic depressive disorder	2426	692	2081	6586	62	1843	30	74	83	36	291	4259	140
(%)	(4.2)	(7.0)	(1.5)	(29.6)	(1.6)	(21.5)	(1.4)	(0.7)	(0.9)	(1.2)	(5.3)	(23.3)	(4.0)
Anxiety	5016	636	9208	3555	294	1211	164	565	466	169	975	2325	270
(%)	(8.7)	(6.5)	(6.4)	(16.0)	(7.4)	(14.1)	(7.7)	(5.4)	(5.1)	(5.4)	(17.7)	(12.7)	(7.7)
Psychosis	516	180	961	634	121	344	30	327	39	27	81	1349	24
(%)	(0.9)	(1.8)	(0.7)	(2.8)	(3.0)	(4.0)	(1.4)	(3.1)	(0.4)	(0.9)	(1.5)	(7.4)	(0.7)
Alcohol and drug abuse or dependence	2195	604	6992	1615	279	851	363	1121	292	85	519	1776	144
(%)	(3.8)	(6.1)	(4.9)	(7.3)	(7.0)	(9.9)	(17.0)	(10.6)	(3.2)	(2.7)	(9.4)	(9.7)	(4.1)
Delirium	183	81	594	149	75	87	26	248	36	11	45	328	21
(%)	(0.3)	(0.8)	(0.4)	(0.7)	(1.9)	(1.0)	(1.2)	(2.4)	(0.4)	(0.4)	(0.8)	(1.8)	(0.6)

eTable 1. Patient characteristics by drug exposure (new treatment episodes) (continued)

	Topiramate	Carbamazepine	Gabapentin	Lamotrigine	Levetiracetam	Oxcarbazepine	Phenobarbital	Phenytoin	Pregabalin	Primidone	Tiagabine	Valproate	Zonisamide
Dementia	239	144	1261	135	187	122	28	566	63	106	35	925	29
(%)	(0.4)	(1.5)	(0.9)	(0.6)	(4.7)	(1.4)	(1.3)	(5.4)	(0.7)	(3.4)	(0.6)	(5.1)	(0.8)
Personality disorder	242	51	363	442	5	175	4	31	16	3	43	290	13
(%)	(0.4)	(0.5)	(0.3)	(2.0)	(0.1)	(2.0)	(0.2)	(0.3)	(0.2)	(0.1)	(0.8)	(1.6)	(0.4)
Sleep disorder	3554	421	7966	1386	209	474	94	359	567	174	529	1020	244
(%)	(6.1)	(4.3)	(5.6)	(6.2)	(5.3)	(5.5)	(4.4)	(3.4)	(6.2)	(5.6)	(9.6)	(5.6)	(6.9)
Other psychiatric disorders	4709	608	6477	3145	306	1385	105	544	314	86	630	2535	298
(%)	(8.1)	(6.2)	(4.5)	(14.1)	(7.7)	(16.1)	(4.9)	(5.2)	(3.5)	(2.8)	(11.5)	(13.9)	(8.4)
Use of other Psychotropic Medications													
Antidepressants	29963	3211	55194	15266	1592	4803	647	2279	3840	1030	3666	10130	1795
(%)	(51.8)	(32.6)	(38.6)	(68.6)	(40.1)	(56.0)	(30.4)	(21.6)	(42.3)	(33.2)	(66.7)	(55.4)	(50.9)
Lithium	823	242	768	2054	34	405	11	20	35	33	97	867	48
(%)	(1.4)	(2.5)	(0.5)	(9.2)	(0.9)	(4.7)	(0.5)	(0.2)	(0.4)	(1.1)	(1.8)	(4.7)	(1.4)
Analgesics	28319	4145	94639	6867	1837	3059	924	4172	6575	1153	3307	6647	1921
(%)	(48.9)	(42.0)	(66.2)	(30.9)	(46.2)	(35.7)	(43.4)	(39.6)	(72.4)	(37.1)	(60.2)	(36.3)	(54.5)
Anti-anxiety	14448	2132	37757	8451	1048	2727	674	1926	2922	878	2476	5928	989
(%)	(25.0)	(21.6)	(26.4)	(38.0)	(26.4)	(31.8)	(31.6)	(18.3)	(32.2)	(28.3)	(45.0)	(32.4)	(28.0)
Hypnotics	7310	948	20395	3887	544	1201	2130	817	1874	316	1306	2412	502
(%)	(12.6)	(9.6)	(14.3)	(17.5)	(13.7)	(14.0)	(100.0)	(7.8)	(20.6)	(10.2)	(23.8)	(13.2)	(14.2)
Antipsychotics	4725	956	6103	5669	273	1806	138	531	439	116	752	4601	262
(%)	(8.2)	(9.7)	(4.3)	(25.5)	(6.9)	(21.1)	(6.5)	(5.0)	(4.8)	(3.7)	(13.7)	(25.1)	(7.4)
Migraine products	20154	579	7471	2105	640	747	125	324	469	83	472	4334	853
(%)	(34.8)	(5.9)	(5.2)	(9.5)	(16.1)	(8.7)	(5.9)	(3.1)	(5.2)	(2.7)	(8.6)	(23.7)	(24.2)
Antiparkinson agents	772	187	2940	480	106	202	29	144	290	258	119	570	88
(%)	(1.3)	(1.9)	(2.1)	(2.2)	(2.7)	(2.4)	(1.4)	(1.4)	(3.2)	(8.3)	(2.2)	(3.1)	(2.5)
ADHD, anti-narcolepsy, anti-obesity, anorexiants	2684	391	3843	3165	163	1039	68	163	332	55	585	1163	221
(%)	(4.6)	(4.0)	(2.7)	(14.2)	(4.1)	(12.1)	(3.2)	(1.5)	(3.7)	(1.8)	(10.6)	(6.4)	(6.3)
Other psychotropic medications	809	287	2796	543	146	255	42	282	254	102	124	836	55
(%)	(1.4)	(2.9)	(2.0)	(2.4)	(3.7)	(3.0)	(2.0)	(2.7)	(2.8)	(3.3)	(2.3)	(4.6)	(1.6)

eTable 1. Patient characteristics by drug exposure (new treatment episodes) (continued)

	Topiramate	Carbamazepine	Gabapentin	Lamotrigine	Levetiracetam	Oxcarbazepine	Phenobarbital	Phenytoin	Pregabalin	Primidone	Tiagabine	Valproate	Zonisamide
Other Comorbidities													
Myocardial infarction or cardiovascular procedure	112	47	1348	49	39	32	15	160	82	35	26	106	15
(%)	(0.2)	(0.5)	(0.9)	(0.2)	(1.0)	(0.4)	(0.7)	(1.5)	(0.9)	(1.1)	(0.5)	(0.6)	(0.4)
Cerebrovascular disease	1447	420	5016	306	696	309	76	2406	330	219	101	824	123
(%)	(2.5)	(4.3)	(3.5)	(1.4)	(17.5)	(3.6)	(3.6)	(22.8)	(3.6)	(7.1)	(1.8)	(4.5)	(3.5)
Other cardiovascular disease**	9667	1972	40736	2773	1152	1318	488	3541	2645	1121	1160	3129	710
(%)	(16.7)	(20.0)	(28.5)	(12.5)	(29.0)	(15.4)	(22.9)	(33.6)	(29.1)	(36.1)	(21.1)	(17.1)	(20.1)
Chronic lung disease	3373	494	10120	1069	265	459	131	744	608	343	340	1106	188
(%)	(5.8)	(5.0)	(7.1)	(4.8)	(6.7)	(5.4)	(6.2)	(7.1)	(6.7)	(11.1)	(6.2)	(6.0)	(5.3)
Diabetes	4224	853	24394	1142	350	497	146	1049	2265	476	400	1216	311
(%)	(7.3)	(8.7)	(17.1)	(5.1)	(8.8)	(5.8)	(6.9)	(10.0)	(24.9)	(15.3)	(7.3)	(6.6)	(8.8)
Hypothyroidism	4203	460	8174	1129	214	408	81	465	516	203	327	829	263
(%)	(7.3)	(4.7)	(5.7)	(5.1)	(5.4)	(4.8)	(3.8)	(4.4)	(5.7)	(6.5)	(5.9)	(4.5)	(7.5)
OA-RA	2675	468	15998	672	249	302	109	508	1068	258	472	713	242
(%)	(4.6)	(4.7)	(11.2)	(3.0)	(6.3)	(3.5)	(5.1)	(4.8)	(11.8)	(8.3)	(8.6)	(3.9)	(6.9)
GI hemorrhage	507	79	1790	158	63	102	32	170	105	52	75	197	50
(%)	(0.9)	(0.8)	(1.3)	(0.7)	(1.6)	(1.2)	(1.5)	(1.6)	(1.2)	(1.7)	(1.4)	(1.1)	(1.4)
Gi inflammatory diseases	245	35	775	88	31	25	8	45	60	15	33	72	19
(%)	(0.4)	(0.4)	(0.5)	(0.4)	(0.8)	(0.3)	(0.4)	(0.4)	(0.7)	(0.5)	(0.6)	(0.4)	(0.5)
Liver cirrhosis and chronic diseases	316	41	1357	103	55	51	44	129	76	22	38	81	20
(%)	(0.5)	(0.4)	(0.9)	(0.5)	(1.4)	(0.6)	(2.1)	(1.2)	(0.8)	(0.7)	(0.7)	(0.4)	(0.6)
Renal failure	81	37	1069	46	45	29	7	148	70	19	13	99	15
(%)	(0.1)	(0.4)	(0.7)	(0.2)	(1.1)	(0.3)	(0.3)	(1.4)	(0.8)	(0.6)	(0.2)	(0.5)	(0.4)
Other renal diseases	159	62	1897	82	52	33	20	142	152	29	18	102	18
(%)	(0.3)	(0.6)	(1.3)	(0.4)	(1.3)	(0.4)	(0.9)	(1.3)	(1.7)	(0.9)	(0.3)	(0.6)	(0.5)
Blood disorders***	183	53	781	67	56	34	12	123	47	17	25	88	16
(%)	(0.3)	(0.5)	(0.5)	(0.3)	(1.4)	(0.4)	(0.6)	(1.2)	(0.5)	(0.5)	(0.5)	(0.5)	(0.5)

* six-months prior to index date

** Other ischemic heart diseases, cardiac arrhythmia, heart failure, hypertension, other cardiologic diseases

*** Aplastic anemia, neutropenia, eosinophilia, thrombocytopenia

eTable 2. Hazard ratios of study outcomes within 180 days*			
	Suicide Attempt	Attempted or Completed Suicide	Attempted or Completed Suicide or Violent Death
REF:TOPIRAMATE	**HR** (95% CI)	**HR** (95% CI)	**HR** (95% CI)
Unadjusted Analysis			
Carbamazepine	0.95 (0.64-1.43)	0.98 (0.66-1.46)	1.05 (0.72-1.54)
Gabapentin	0.84 (0.70-1.01)	0.85 (0.71-1.02)	0.89 (0.74-1.06)
Lamotrigine	3.63 (2.97-4.44)	3.72 (3.05-4.54)	3.71 (3.05-4.51)
Levetiracetam	1.27(0.74-2.19)	1.26 (0.73-2.16)	1.48 (0.90-2.44)
Oxcarbazepine	4.18(3.27-5.35)	4.25 (3.33-5.42)	4.28 (3.37-5.44)
Phenobarbital	1.96(1.09-3.52)	1.93 (1.08-3.47)	1.88 (1.05-3.37)
Phenytoin	0.83(0.55-1.26)	0.85 (0.57-1.29)	0.96 (0.65-1.41)
Pregabalin	0.61(0.35-1.07)	0.60 (0.34-1.06)	0.72 (0.43-1.20)
Primidone	0.34(0.11-1.05)	0.44 (0.16-1.19)	0.64 (0.29-1.45)
Tiagabine	3.28(2.41-4.46)	3.24 (2.38-4.40)	3.26 (2.41-4.41)
Valproate	3.09(2.49-3.84)	3.17 (2.56-3.93)	3.21 (2.60-3.96)
Zonisamide	1.16(0.65-2.09)	1.15 (0.64-2.06)	1.30 (0.75-2.24)
Age-, sex-, and calendar year-adjusted analysis			
Carbamazepine	1.11(0.74-1.67)	1.11 (0.74-1.66)	1.16 (0.79-1.71)
Gabapentin	1.30(1.07-1.57)	1.28 (1.06-1.55)	1.27 (1.05-1.53)
Lamotrigine	3.27(2.66-4.00)	3.34 (2.73-4.08)	3.34 (2.74-4.07)
Levetiracetam	1.46(0.85-2.52)	1.42 (0.82-2.45)	1.63 (0.99-2.69)
Oxcarbazepine	3.48(2.71-4.47)	3.50 (2.74-4.48)	3.53 (2.76-4.50)
Phenobarbital	2.37(1.32-4.26)	2.29 (1.27-4.12)	2.14 (1.19-3.85)
Phenytoin	1.05(0.69-1.60)	1.04 (0.69-1.58)	1.11 (0.75-1.65)
Pregabalin	1.28(0.72-2.27)	1.23 (0.69-2.18)	1.35 (0.80-2.27)
Primidone	0.71(0.22-2.22)	0.89 (0.33-2.39)	1.12 (0.49-2.54)
Tiagabine	3.74(2.74-5.10)	3.61 (2.65-4.92)	3.57 (2.63-4.84)
Valproate	2.85(2.28-3.56)	2.86 (2.29-3.56)	2.84 (2.29-3.53)
Zonisamide	1.25 (0.70-2.25)	1.23 (0.69-2.21)	1.38 (0.80-2.39)

eTable 2. Hazard ratios of study outcomes within 180 days (continued)

	Suicide Attempt	Attempted or Completed Suicide	Attempted or Completed Suicide or Violent Death
REF:TOPIRAMATE	**HR** (95% CI)	**HR** (95% CI)	**HR** (95% CI)
Adjusted analysis**			
Carbamazepine	0.99 (0.66-1.50)	1.00 (0.66-1.50)	1.05 (0.71-1.55)
Gabapentin	1.33 (1.09-1.62)	1.32 (1.08-1.60)	1.31 (1.08-1.58)
Lamotrigine	1.63 (1.31-2.02)	1.67 (1.35-2.07)	1.71 (1.39-2.11)
Levetiracetam	1.55 (0.89-2.71)	1.50 (0.86-2.62)	1.68 (1.01-2.79)
Oxcarbazepine	1.84 (1.43-2.38)	1.86 (1.45-2.40)	1.92 (1.49-2.46)
Phenobarbital	1.30 (0.71-2.37)	1.24 (0.68-2.27)	1.20 (0.66-2.19)
Phenytoin	1.18 (0.74-1.88)	1.15 (0.73-1.82)	1.17 (0.76-1.80)
Pregabalin	1.18 (0.66-2.10)	1.15 (0.65-2.06)	1.28 (0.75-2.16)
Primidone	0.84 (0.26-2.71)	1.06 (0.38-2.95)	1.37 (0.58-3.21)
Tiagabine	2.11 (1.54-2.89)	2.05 (1.50-2.81)	2.07 (1.52-2.82)
Valproate	0.99 (0.66-1.50)	1.53 (1.22-1.92)	1.54 (1.23-1.92)
Zonisamide	1.33 (1.09-1.62)	1.29 (0.72-2.32)	1.44 (0.84-2.49)

* Cumulative risk analysis carrying forward the first drug exposure until day 180

** Hazard ratios were adjusted in a Cox proportional hazard regression for age, sex, calendar year, initiation anticonvulsant medication initiated, depression, manic disorder, psychotic disorder, anxiety, alcohol abuse or dependence, drug abuse or dependence, delirium, dementia, personality disorder, sleep disorder, other psychiatric disorder, epilepsy, seizure disorder, neuropathy and neuropathic pain, migraine, tremor, multiple sclerosis, head injury, Parkinson disease, amyotrophic lateral sclerosis, number of drug, previous hospitalization, previous ambulatory visit, previous hospitalization for epilepsy or seizure disorder, previous hospitalization for mood disorder, previous hospitalization for any psychiatric disorder, antidepressants, lithium, antipsychotics, anxiolytics, analgesics, migraine medications, hypnotics, other psychotropic medications, myocardial infarction or revascularization procedure, cerebrovascular disease, other cardiovascular diseases, diabetes mellitus, chronic lung diseases, hypothyroidism, osteoarthritis or rheumatoid arthritis, GI hemorrhage and inflammatory diseases, liver cirrhosis and chronic diseases, renal failure and other renal diseases, blood disorders.

eTable 3. Study population, follow-up, and event rates

	Participants	Episodes	Mean Follow-up (SD)	Median Follow-up; [25th;75th]	Events within 360 days (Incidence Rates per 1,000 person-years)*			
					Attempted Suicide n=905	Completed Suicide n=29	Attempted or Completed Suicide n=933	Attempted or Completed Suicide or Violent Death n=982
Topiramate**	52127	57853	122 (100)	60 [60;152]	129 (6.7)	2 (0.1)	131 (6.8)	136 (7.1)
Carbamazepine	8778	9859	105 (93)	60 [60;120]	23 (8.1)	1 (0.4)	24 (8.4)	25 (8.8)
Ethosuximide	42	47	90 (81)	60 [60;60]	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Felbamate	13	15	138 (120)	66 [60;227]	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gabapentin	130698	142865	100 (86)	60 [60;111]	249 (6.3)	9 (0.2)	257 (6.5)	275 (7.0)
Lamotrigine	20062	22256	145 (113)	98 [60;215]	212(23.9)	8 (0.9)	220(24.8)	226(25.5)
Levetiracetam	3544	3975	119 (101)	60 [60;146]	11 (8.5)	0 (0.0)	11 (8.5)	12 (9.3)
Oxcarbazepine	7725	8579	123 (101)	67 [60;154]	83 (28.8)	2 (0.7)	85 (29.5)	88 (30.5)
Phenobarbital	1859	2130	88 (90)	60 [37;90]	5 (9.7)	0 (0.0)	5 (9.7)	5 (9.7)
Phenytoin	9833	10531	127 (109)	66 [60;164]	22 (6.0)	1 (0.3)	23 (6.3)	24 (6.5)
Pregabalin	7875	9086	83 (66)	60 [50;97]	9 (4.4)	0 (0.0)	9 (4.4)	12 (5.8)
Primidone	2871	3104	122 (105)	60 [60;150]	2 (1.9)	1 (1.0)	3 (2.9)	6 (5.8)
Tiagabine	4853	5497	103 (85)	60 [60;120]	39 (25.1)	0 (0.0)	39 (25.1)	40 (25.8)
Valproate	16692	18295	111 (92)	60 [60;127]	113(20.3)	5 (0.9)	118(21.2)	124(22.3)
Zonisamide	2965	3528	109 (92)	60 [60;120]	8 (7.6)	0 (0.0)	8 (7.6)	9 (8.5)

* As treated analysis censoring at termination of health plan eligibility, treatment discontinuation, switching , event, or at 180 days whichever comes first
** Reference drug

eTable 4. Hazard ratios of study outcomes within 360 days*			
	Suicide Attempt	Attempted or Completed Suicide	Attempted or Completed Suicide or Violent Death
REF:TOPIRAMATE	**HR** (95% CI)	**HR** (95% CI)	**HR** (95% CI)
Unadjusted Analysis			
Carbamazepine	1.17 (0.75-1.82)	1.20 (0.78-1.85)	1.21 (0.79-1.85)
Gabapentin	0.90 (0.73-1.11)	0.91 (0.74-1.13)	0.95 (0.77-1.16)
Lamotrigine	3.76 (3.02-4.68)	3.85 (3.10-4.78)	3.79 (3.07-4.69)
Levetiracetam	1.27 (0.69-2.35)	1.25 (0.68-2.31)	1.31 (0.73-2.37)
Oxcarbazepine	4.32 (3.28-5.69)	4.35 (3.31-5.72)	4.34 (3.32-5.68)
Phenobarbital	1.36 (0.56-3.33)	1.34 (0.55-3.28)	1.30 (0.53-3.17)
Phenytoin	0.91 (0.58-1.44)	0.94 (0.60-1.47)	0.95 (0.61-1.46)
Pregabalin	0.59 (0.30-1.16)	0.58 (0.29-1.14)	0.75 (0.41-1.35)
Primidone	0.29 (0.07-1.17)	0.43 (0.14-1.35)	0.83 (0.36-1.87)
Tiagabine	3.57 (2.49-5.11)	3.51 (2.46-5.02)	3.48 (2.45-4.95)
Valproate	2.96 (2.30-3.81)	3.04 (2.37-3.90)	3.09 (2.42-3.94)
Zonisamide	1.10 (0.54-2.24)	1.08 (0.53-2.21)	1.17 (0.60-2.30)
Age-, sex-, and calendar year-adjusted analysis			
Carbamazepine	1.36 (0.87-2.12)	1.36 (0.88-2.11)	1.35 (0.88-2.07)
Gabapentin	1.47 (1.18-1.83)	1.44 (1.16-1.80)	1.45 (1.17-1.79)
Lamotrigine	3.48 (2.79-4.35)	3.56 (2.86-4.43)	3.52 (2.83-4.36)
Levetiracetam	1.51 (0.82-2.80)	1.47 (0.79-2.72)	1.52 (0.84-2.74)
Oxcarbazepine	3.71 (2.80-4.91)	3.70 (2.80-4.88)	3.70 (2.82-4.86)
Phenobarbital	1.74 (0.71-4.26)	1.67 (0.68-4.09)	1.58 (0.65-3.86)
Phenytoin	1.27 (0.80-2.00)	1.25 (0.80-1.96)	1.22 (0.79-1.90)
Pregabalin	1.25 (0.63-2.49)	1.20 (0.61-2.38)	1.46 (0.80-2.67)
Primidone	0.67 (0.16-2.70)	0.93 (0.30-2.94)	1.66 (0.73-3.78)
Tiagabine	4.14 (2.88-5.95)	3.98 (2.77-5.71)	3.90 (2.73-5.58)
Valproate	2.90 (2.23-3.76)	2.90 (2.25-3.75)	2.92 (2.27-3.75)
Zonisamide	1.16 (0.57-2.38)	1.14 (0.56-2.33)	1.23 (0.63-2.42)

eTable 4. Hazard ratios of study outcomes within 360 days (continued)			
	Suicide Attempt	Attempted or Completed Suicide	Attempted or Completed Suicide or Violent Death
REF:TOPIRAMATE	**HR** (95% CI)	**HR** (95% CI)	**HR** (95% CI)
Adjusted analysis*			
Carbamazepine	1.25 (0.79-1.96)	1.25 (0.80-1.95)	1.24 (0.80-1.92)
Gabapentin	1.39 (1.10-1.74)	1.37 (1.09-1.72)	1.37 (1.10-1.71)
Lamotrigine	1.78 (1.41-2.26)	1.83 (1.45-2.31)	1.84 (1.46-2.32)
Levetiracetam	1.66 (0.88-3.11)	1.59 (0.85-2.98)	1.60 (0.87-2.92)
Oxcarbazepine	2.02 (1.52-2.70)	2.03 (1.52-2.70)	2.06 (1.55-2.73)
Phenobarbital	1.18 (0.48-2.92)	1.11 (0.45-2.75)	1.07 (0.43-2.65)
Phenytoin	1.34 (0.80-2.24)	1.31 (0.80-2.17)	1.22 (0.75-1.99)
Pregabalin	1.09 (0.55-2.19)	1.07 (0.53-2.13)	1.29 (0.71-2.38)
Primidone	0.72 (0.17-3.01)	1.01 (0.31-3.31)	1.88 (0.79-4.47)
Tiagabine	2.27 (1.57-3.28)	2.20 (1.52-3.17)	2.18 (1.52-3.14)
Valproate	1.57 (1.20-2.05)	1.56 (1.20-2.04)	1.59 (1.22-2.06)
Zonisamide	1.27 (0.62 2.60)	1.25 (0.61-2.55)	1.34 (0.68-2.63)

* As treated analysis censoring at termination of health plan eligibility, treatment discontinuation, switching , event, or at 360 days whichever comes first
** Hazard ratios were adjusted in a Cox proportional hazard regression for age, sex, calendar year, initiation anticonvulsant medication initiated, depression, manic disorder, psychotic disorder, anxiety, alcohol abuse or dependence, drug abuse or dependence, delirium, dementia, personality disorder, sleep disorder, other psychiatric disorder, epilepsy, seizure disorder, neuropathy and neuropathic pain, migraine, tremor, multiple sclerosis, head injury, Parkinson disease, amyotrophic lateral sclerosis, number of drug, previous hospitalization, previous ambulatory visit, previous hospitalization for epilepsy or seizure disorder, previous hospitalization for mood disorder, previous hospitalization for any psychiatric disorder, antidepressants, lithium, antipsychotics, anxiolytics, analgesics, migraine medications, hypnotics, other psychotropic medications, myocardial infarction or revascularization procedure, cerebrovascular disease, other cardiovascular diseases, diabetes mellitus, chronic lung diseases, hypothyroidism, osteoarthritis or rheumatoid arthritis, GI hemorrhage and inflammatory diseases, liver cirrhosis and chronic diseases, renal failure and other renal diseases, blood disorders.

eTable 5. Matched population and event rates

Matched Group Vs Topiramate	Matched Treatment Episodes***	As Treated Analysis* Events within 180 days (Incidence Rates per 1000 person-years)			Carried Forward Analysis** Events within 180 days (Incidence Rates per 1000 person-years)		
		Person-years	Attempted or Completed Suicide	Attempted or Completed Suicide or Violent Death	Person-years	Attempted or Completed Suicide	Attempted or Completed Suicide or Violent Death
Carbamazepine	15994	1885	18 (9.5)	18 (9.5)	3368	23 (6.8)	25 (7.4)
Topiramate		2028	18 (8.9)	18 (8.9)	3355	33 (9.8)	34 (10.1)
Gabapentin	81612	9328	105 (11.3)	111 (11.9)	17237	151 (8.8)	160 (9.3)
Topiramate		10774	61 (5.7)	64 (5.9)	17219	104 (6.0)	108 (6.3)
Lamotrigine	29494	4365	101 (23.1)	104 (23.8)	5924	131 (22.1)	135 (22.8)
Topiramate		3862	68 (17.6)	70 (18.1)	6192	105 (17.0)	108 (17.4)
Levetiracetam	7758	1003	10 (10.0)	11 (11.0)	1568	14 (8.9)	17 (10.8)
Topiramate		999	16 (16.0)	18 (18.0)	1622	22 (13.6)	24 (14.8)
Oxcarbazepine	15784	2108	64 (30.4)	67 (31.8)	3323	90 (27.1)	94 (28.3)
Topiramate		2063	42 (20.4)	42 (20.4)	3310	61 (18.4)	61 (18.4)
Phenobarbital	4050	406	4 (9.8)	4 (9.8)	856	10 (11.7)	10 (11.7)
Topiramate		500	3 (6.0)	3 (6.0)	844	6 (7.1)	6 (7.1)
Phenytoin	8880	1149	6 (5.2)	6 (5.2)	1866	10 (5.4)	10 (5.4)
Topiramate		1103	4 (3.6)	4 (3.6)	1851	4 (2.2)	5 (2.7)
Pregabalin***	10914	1137	6 (5.3)	8 (7.0)	1829	8 (4.4)	10 (5.5)
Topiramate		1341	8 (6.0)	8 (6.0)	2150	10 (4.7)	10 (4.7)
Primidone	3886	496	3 (6.0)	5 (10.1)	815	4 (4.9)	6 (7.4)
Topiramate		505	3 (5.9)	3 (5.9)	824	3 (3.6)	3 (3.6)
Tiagabine	10822	1304	37 (28.4)	38 (29.1)	2394	53 (22.1)	55 (23.0)
Topiramate		1398	20 (14.3)	20 (14.3)	2322	33 (14.2)	33 (14.2)
Valproate	4608	567	9 (15.9)	9 (15.9)	966	12 (12.4)	12 (12.4)
Topiramate		639	12 (18.8)	13 (20.3)	974	18 (18.5)	19 (19.5)
Zonisamide	7036	871	7 (8.0)	8 (9.2)	1515	12 (7.9)	14 (9.2)
Topiramate		929	2 (2.2)	2 (2.2)	1481	4 (2.7)	4 (2.7)

* As treated analysis censoring at termination of health plan eligibility, treatment discontinuation, switching , event, or at 180 days whichever comes first
** Cumulative risk analysis carrying forward the first drug exposure until day 180
*** Size of successfully matched patients in the topiramate and individual drug combined
**** Restricted to 2005-2006

eTable 6. High-Dimension Propensity Score 1:1 matched analysis of events within 180 days				
Reference Drug: TOPIRAMATE	Attempted or Completed Suicide		Attempted or Completed Suicide or Violent Death	
	RR (95% CI)	RD per 1,000 person-years (95% CI)	RR (95% CI)	RD per 1,000 person-years (95% CI)
As Treated Analysis*				
Carbamazepine n = 15,994**	1.08 (0.56;2.08)	0.67 (-5.35;6.69)	1.08 (0.56;2.08)	0.67 (-5.35;6.69)
Gabapentin n = 81,612	1.99 (1.45;2.73)	5.59 (3.01;8.17)	2.00 (1.47;2.72)	5.96 (3.31;8.61)
Lamotrigine n = 29,494	1.31 (0.96;1.78)	5.53 (-0.62;11.68)	1.31 (0.97;1.77)	5.70 (-0.54;11.94)
Levetiracetam n = 7,758	0.62 (0.28;1.37)	-6.05 (-16.04;3.94)	0.61 (0.29;1.29)	-7.06 (-17.61;3.49)
Oxcarbazepine n = 15,784	1.49 (1.01;2.20)	10 (0.35;19.65)	1.56 (1.06;2.29)	11.42 (1.63;21.21)
Phenobarbital n = 4,050	1.64 (0.37;7.33)	3.84 (-7.96;15.64)	1.64 (0.37;7.33)	3.84 (-7.96;15.64)
Phenytoin n = 8,880	1.44 (0.41;5.10)	1.59 (-3.90;7.08)	1.44 (0.41;5.10)	1.59 (-3.9;7.08)
Pregabalin n = 10,914	0.88 (0.31;2.54)	-0.69 (-6.60;5.22)	1.18 (0.44;3.14)	1.07 (-5.32;7.46)
Primidone n = 3,886	1.02 (0.21;5.05)	0.10 (-9.49;9.69)	1.69 (0.40;7.07)	4.13 (-6.97;15.23)
Tiagabine n = 10,822	1.98 (1.15;3.41)	14.06 (2.97;25.15)	2.04 (1.19;3.51)	14.83 (3.64;26.02)
Valproate n = 4,608	0.84 (0.35;1.99)	-2.92 (-17.76;11.92)	0.78 (0.33;1.82)	-4.48 (-9.64;10.68)
Zonisamide n = 7,036	3.73 (0.77;17.96)	5.88 (-0.78;12.54)	4.26 (0.90;20.06)	7.03 (0.00;14.06)

eTable 6. High-Dimension Propensity Score 1:1 matched analysis of events within 180 days (continued)

Reference Drug: TOPIRAMATE	Attempted or Completed Suicide		Attempted or Completed Suicide or Violent Death	
	RR (95% CI)	RD per 1,000 person-years (95% CI)	RR (95% CI)	RD per 1,000 person-years (95% CI)
Cumulative Risk Analysis***				
Carbamazepine n = 15,994**	0.69 (0.41;1.18)	-3.01 (-7.37;1.35)	0.73 (0.44;1.22)	-2.71 (-7.19;1.77)
Gabapentin n = 81,612	1.45 (1.13;1.86)	2.72 (0.90;4.54)	1.48 (1.16;1.89)	3.01 (1.15;4.87)
Lamotrigine n = 29,494	1.3 (1.01;1.68)	5.16 (0.17;10.15)	1.31 (1.02;1.69)	5.35 (0.29;10.41)
Levetiracetam n = 7,758	0.66 (0.34;1.29)	-4.63 (-11.98;2.72)	0.73 (0.39;1.36)	-3.95 (-11.80;3.90)
Oxcarbazepine n = 15,784	1.47 (1.06;2.03)	8.66 (1.40;15.92)	1.53 (1.11;2.11)	9.86 (2.50;17.22)
Phenobarbital n = 4,050	1.64 (0.60;4.51)	4.57 (-4.64;13.78)	1.64 (0.60;4.51)	4.57 (-4.64;13.78)
Phenytoin n = 8,880	2.48 (0.78;7.91)	3.2 (-0.74;7.14)	1.98 (0.68;5.79)	2.66 (-1.42;6.74)
Pregabalin n = 10,914	0.94 (0.37;2.38)	-0.28 (-4.46;3.90)	1.18 (0.49;2.84)	0.82 (-3.63;5.27)
Primidone n = 3,886	1.35 (0.30;6.03)	1.26 (-5.07;7.59)	2.02 (0.51;8.08)	3.72 (-3.47;10.91)
Tiagabine n = 10,822	1.56 (1.01;2.41)	7.93 (0.25;15.61)	1.62 1.05;2.49)	8.76 (0.99;16.53)
Valproate n = 4,608	0.67 (0.32;1.39)	-6.05 (-17.11;5.01)	0.64 0.31;1.32)	-7.08 (-18.32;4.16)
Zonisamide n = 7,036	2.93 (0.94;9.08)	5.22 (0.02;10.42)	3.42 1.13;10.39)	6.54 (1.02;12.06)

* As treated analysis censoring at termination of health plan eligibility, treatment discontinuation, switching , event, or at 180 days whichever comes first
** Size of successfully matched patients in the topiramate and individual drug combined
*** Analysis carrying forward the first drug exposure until day 180

eTable 7. High-dimension propensity score 1:1 matched analysis of events within 360 days

Reference Drug: TOPIRAMATE	Attempted or Completed Suicide		Attempted or Completed Suicide or Violent Death	
	RR (95% CI)	RD per 1,000 person-years (95% CI)	RR (95% CI)	RD per 1,000 person-years (95% CI)
As Treated Analysis*				
Carbamazepine n = 15,994**	1.26 (0.67;2.36)	1.88 (-3.31;7.07)	1.19 (0.64;2.21)	1.47 (-3.78;6.72)
Gabapentin n = 81,612	1.89 (1.41;2.53)	4.94 (2.65;7.23)	1.89 (1.42;2.51)	5.19 (2.84;7.54)
Lamotrigine n = 29,494	1.28 (0.96;1.7)	4.58 (-0.64;9.8)	1.26 (0.95;1.67)	4.46 (-0.84;9.76)
Levetiracetam n = 7,758	0.59 (0.28;1.25)	-5.96 (-14.5;2.58)	0.58 (0.28;1.19)	-6.8 (-15.77;2.17)
Oxcarbazepine n = 15,784	1.49 (1.03;2.15)	9.12 (0.82;17.42)	1.52 (1.06;2.18)	9.87 (1.43;18.31)
Phenobarbital n = 4,050	2.04 (0.49;8.54)	5.16 (-5.37;15.69)	2.04 (0.49;8.54)	5.16 (-5.37;15.69)
Phenytoin n = 8,880	2.25 (0.71;7.17)	3.77 (-1.38;8.92)	1.8 (0.62;5.27)	3.01 (-2.35;8.37)
Pregabalin n = 10,914	0.86 (0.31;2.42)	-0.82 (-6.18;4.54)	1.14 (0.44;2.95)	0.8 (-5.01;6.61)
Primidone n = 3,886	0.98 (0.2;4.86)	-0.1 (-7.84;7.64)	1.63 (0.39;6.82)	3.09 (-5.82;12)
Tiagabine n = 10,822	1.93 (1.14;3.26)	11.97 (2.43;21.51)	1.98 (1.17;3.34)	12.62 (2.99;22.25)
Valproate n = 4,608	0.73 (0.32;1.67)	-5.04 (-17.75;7.67)	0.68 (0.30;1.54)	-6.26 (-19.19;6.67)
Zonisamide n = 7,036	2.93 (0.78;11.04)	5.01 (-1.02;11.04)	3.3 (0.89;12.19)	5.96 (-0.35;12.27)

* As treated analysis censoring at termination of health plan eligibility, treatment discontinuation, switching , event, or at 180 days whichever comes first
** Size of successfully matched patients

eTable 8. Hazard ratios of study outcomes within 30 days*

	Suicide Attempt	Attempted or Completed Suicide	Attempted or Completed Suicide or Violent Death
REF:TOPIRAMATE	**HR** (95% CI)	**HR** (95% CI)	**HR** (95% CI)
Adjusted analysis**			
Carbamazepine	1.87 (0.94-3.73)	2.02 (1.04-3.93)	1.97 (1.01-3.82)
Gabapentin	1.68 (1.12-2.52)	1.73 (1.15-2.58)	1.68 (1.13-2.5)
Lamotrigine	2.45 (1.6-3.76)	2.56 (1.67-3.90)	2.55 (1.68-3.88)
Levetiracetam	3.34 (1.38-8.09)	3.30 (1.36-7.99)	3.59 (1.57-8.21)
Oxcarbazepine	2.79 (1.7-4.55)	2.74 (1.68-4.48)	2.89 (1.79-4.67)
Phenobarbital	0.46 (0.06-3.43)	0.46 (0.06-3.37)	0.45 (0.06-3.29)
Phenytoin	2.42 (1.12-5.2)	2.39 (1.11-5.15)	2.34 (1.12-4.9)
Pregabalin	1.98 (0.75-5.18)	2.02 (0.77-5.29)	1.87 (0.71-4.89)
Primidone	1.63 (0.21-12.53)	1.46 (0.19-11.21)	4.29 (1.22-15.05)
Tiagabine	3.57 (2.02-6.33)	3.52 (1.99-6.24)	3.39 (1.92-5.99)
Valproate	1.61 (1-2.6)	1.64 (1.02-2.64)	1.76 (1.11-2.79)
Zonisamide	2.21 (0.78-6.22)	2.21 (0.78-6.22)	2.11 (0.75-5.93)

* As treated analysis censoring at termination of health plan eligibility, treatment discontinuation, switching , event, or at 180 days whichever comes first

** Hazard ratios were adjusted in a Cox proportional hazard regression for age, sex, calendar year, initiation anticonvulsant medication initiated, depression, manic disorder, psychotic disorder, anxiety, alcohol abuse or dependence, drug abuse or dependence, delirium, dementia, personality disorder, sleep disorder, other psychiatric disorder, epilepsy, seizure disorder, neuropathy and neuropathic pain, migraine, tremor, multiple sclerosis, head injury, Parkinson disease, amyotrophic lateral sclerosis, number of drug, previous hospitalization, previous ambulatory visit, previous hospitalization for epilepsy or seizure disorder, previous hospitalization for mood disorder, previous hospitalization for any psychiatric disorder, antidepressants, lithium, antipsychotics, anxiolytics, analgesics, migraine medications, hypnotics, other psychotropic medications, myocardial infarction or revascularization procedure, cerebrovascular disease, other cardiovascular diseases, diabetes mellitus, chronic lung diseases, hypothyroidism, osteoarthritis or rheumatoid arthritis, GI hemorrhage and inflammatory diseases, liver cirrhosis and chronic diseases, renal failure and other renal diseases, blood disorders.

eTable 9. Propensity score 1:1 matched analysis of attempted suicides within 180 days*					
Reference Drug: **CARBAMAZEPINE**	Matched treatment episodes	Attempted Suicides	Person-years	RR (95% CI)	RD per 1,000 person-years (95% CI)
Gabapentin	18380	45	3417	1.45 (0.92;2.29)	4.08 (-0.93;9.08)
Carbamazepine		31	3409		
Lamotrigine	11574	30	2114	0.97 (0.59;1.61)	0.40 (-6.83;7.62)
Carbamazepine		31	2126		
Levetiracetam	6268	11	1160	1.10 (0.47;2.58])	0.82 (-6.94;8.59)
Carbamazepine		10	1155		
Oxcarbazepine	11120	46	2116	1.41 (0.90;2.21)	6.28 (-1.98;14.54)
Carbamazepine		32	2069		
Phenobarbital	4144	10	764	1.12 (0.45;2.75)	1.36 (-9.80;12.52)
Carbamazepine		9	767		
Phenytoin	9984	16	1866	2.62 (1.03;6.70)	5.30 (0.35;10.25)
Carbamazepine		6	1834		
Pregabalin	5266	3	840	0.63 (0.15;2.65)	2.07 (-4.32;8.46)
Carbamazepine		5	886		
Primidone	5114	3	954	0.98 (0.20;4.88)	0.05 (-5.02;5.13)
Carbamazepine		3	938		
Tiagabine	6876	31	1379	1.23 (0.72;2.09)	4.16 (-6.63;14.94)
Carbamazepine		24	1310		
Topiramate	16616	26	3122	0.80 (0.48;1.34)	2.07 (-2.75;6.89)
Carbamazepine		32	3077		
Valproate	13758	33	2517	1.02 (0.63;1.65)	0.21 (-6.06;6.49)
Carbamazepine		33	2558		
Zonisamide	5704	10	1114	0.97 (0.40;2.32)	0.34 (-7.68;8.35)
Carbamazepine		10	1074		
* As treated analysis censoring at termination of health plan eligibility, treatment discontinuation, switching , event, or at 180 days whichever comes first					

eTable 10. Propensity score 1:1 matched subgroup analysis of attempted suicides within 180 days in selected patient populations*				
Reference Drug: **CARBAMAZEPINE**	Attempted Suicides	Person-years	RR (95% CI)	RD per 1,000 person-years (95% CI)
15-24 years				
Gabapentin	7	280	1.42 (0.48;4.22)	7.37 (-15.95;30.69)
Carbamazepine	6	340		
Lamotrigine	11	336	1.59 (0.62;4.11)	12.19 (-12.40;36.78)
Carbamazepine	7	341		
Oxcarbazepine	16	404	2.04 (0.84;4.97)	20.24 (-3.90;44.38)
Carbamazepine	7	361		
Phenytoin	2	194	2.28 (0.21;25.12)	5.79 (-11.04;22.62)
Carbamazepine	1	221		
Topiramate	4	260	0.93 (0.26;3.31)	1.10 (-18.95;21.14)
Carbamazepine	6	364		
Valproate	15	388	2.05 (0.84;5.04)	19.82 (-4.18;43.83)
Carbamazepine	7	372		
25-64 years				
Gabapentin	25	2660	1.32 (0.79;2.21)	3.04 (-2.49;8.57)
Carbamazepine	35	2813		
Lamotrigine	24	1645	0.78 (0.42;1.42)	3.29 (-4.45;11.03)
Carbamazepine	19	1681		
Oxcarbazepine	30	1577	1.19 (0.70;2.03)	3.26 (-5.94;12.45)
Carbamazepine	25	1586		
Phenytoin	5	1361	2.70 (0.97;7.50)	6.24 (0.13;12.34)
Carbamazepine	14	1413		
Topiramate	26	2405	0.77 (0.43;1.35)	2.55 (-2.86;7.95)
Carbamazepine	22	2662		
Valproate	26	1973	0.73 (0.40;1.34)	3.52 (-3.24;10.27)
Carbamazepine	18	1863		
With mood disorder				
Gabapentin	27	591	1.22 (0.73;2.03)	10.00 (-15.66;35.66)
Carbamazepine	33	592		
Lamotrigine	29	585	0.51 (0.27;0.95)	24.23 (2.06;46.39)
Carbamazepine	15	591		
Oxcarbazepine	29	588	1.01 (0.60;1.68)	0.27 (-25.19;25.73)
Carbamazepine	29	585		

eTable 10. Propensity score 1:1 matched subgroup analysis of attempted suicides within 180 days in selected patient populations (continued)				
Reference Drug: **CARBAMAZEPINE**	Attempted Suicides	Person-years	RR (95% CI)	RD per 1,000 person-years (95% CI)
Phenytoin	6	182	1.60 (0.58;4.41)	19.92 (-22.16;61.99)
Carbamazepine	10	189		
Topiramate	28	581	0.66 (0.37;1.18)	16.32 (-6.57;39.22)
Carbamazepine	19	596		
Valproate	29	588	0.61 (0.34;1.11)	19.20 (-3.75;42.15)
Carbamazepine	17	565		
With epilepsy or seizure disorder				
Gabapentin	1	291	13.92 (1.82;106.38)	44.43 (17.55;71.31)
Carbamazepine	13	272		
Lamotrigine	3	271	---	11.09 (-1.46;23.64)
Carbamazepine	0	289		
Oxcarbazepine	4	323	0.73 (0.16;3.28)	3.31 (-12.61;19.23)
Carbamazepine	3	330		
Phenytoin	3	493	3.48 (0.97;12.47)	15.10 (0.81;29.40)
Carbamazepine	11	519		
Topiramate	28	682	0.67 (0.37;1.19)	13.70 (-5.86;33.26)
Carbamazepine	19	695		
Valproate	4	341	0.49 (0.09;2.70)	5.93 (-8.08;19.94)
Carbamazepine	2	346		

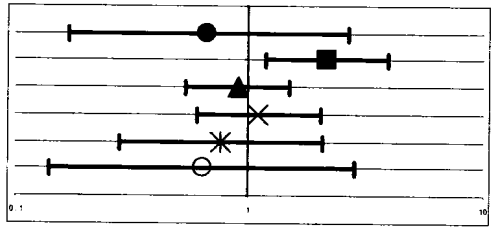
* As treated analysis censoring at termination of health plan eligibility, treatment discontinuation, switching , event, or at 180 days whichever comes first
** Size of successfully matched patients

eFigure. Subgroup analyses in selected patient populations after high-dimension propensity score matching**

15-24 year-old Population

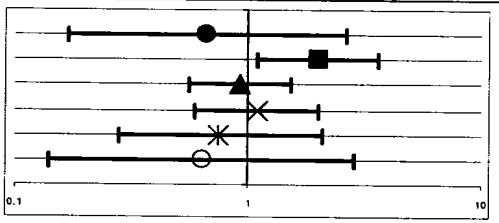
REF: Topiramate	RR [95% CI]	Sample Sizes*
Carbamazepine	0.67 [0.17-2.68]	4/265; 4/176
Gabapentin	2.15 [1.18-3.92]	37/839; 15/732
Lamotrigine	0.90 [0.54-1.50]	32/817; 27/622
Oxcarbazepine	1.11 [0.60-2.05]	26/546; 17/396
Tiagabine	0.76 [0.28-2.10]	7/120; 8/104
Valproate	0.64 [0.14-2.86]	3/93; 4/78

Attempted or Completed Suicide



REF: Topiramate	RR [95% CI]	Sample Sizes*
Carbamazepine	0.67 [0.17-2.68]	4/265; 4/176
Gabapentin	2.02 [1.12-3.63]	37/839; 16/732
Lamotrigine	0.93 [0.56-1.55]	33/ 817; 27/622
Oxcarbazepine	1.11 [0.60-2.05]	26/546; 17/396
Tiagabine	0.76 [0.28-2.10]	7/120; 8/104
Valproate	0.64 [0.14-2.86]	3/93; 4/78

Attempted or Completed Suicide or Violent Death



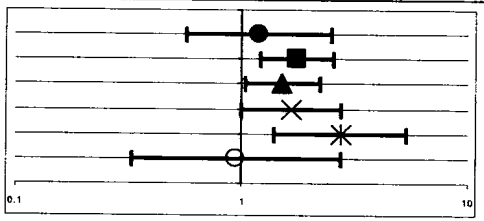
Carbamazepine
Gabapentin
Lamotrigine
Oxcarbazepine
Tiagabine
Valproate

*Drug events/PY; Reference drug events/PY

25-64 year-old Population

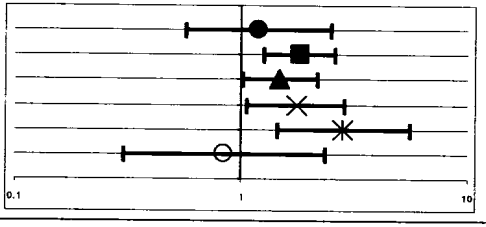
REF: Topiramate	RR [95% CI]	Sample Sizes*
Carbamazepine	1.21 [0.58-2.54]	14/1437; 14/1733
Gabapentin	1.78 [1.22-2.59]	68/8078; 46/9727
Lamotrigine	1.58 [1.04-2.25]	68/3441; 41/3172
Oxcarbazepine	1.67 [1.01-2.77]	38/1479; 25/1625
Tiagabine	2.75 [1.41-5.37]	30/1123; 12/1234
Valproate	0.96 [0.33-2.77]	6/428; 8/545

Attempted or Completed Suicide



REF: Topiramate	RR [95% CI]	Sample Sizes*
Carbamazepine	1.21 [0.58-2.54]	14/1437; 14/1733
Gabapentin	1.83 [1.27-2.63]	73/8078; 48/9727
Lamotrigine	1.50 [1.03-2.19]	70/3441; 43/3172
Oxcarbazepine	1.76 [1.07-2.90]	40/1479; 25/1625
Tiagabine	2.84 [1.46-5.53]	31/1123; 12/1234
Valproate	0.85 [0.30-2.39]	6/428; 9/545

Attempted or Completed Suicide or Violent Death



Carbamazepine
Gabapentin
Lamotrigine
Oxcarbazepine
Tiagabine
Valproate

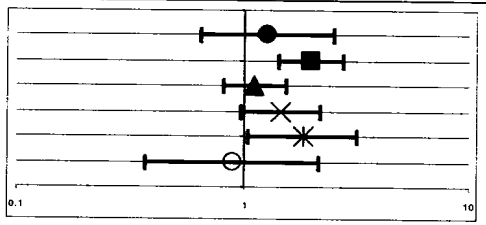
*Drug events/PY; Reference drug events/PY

eFigure. Subgroup analyses in selected patient populations after high-dimension propensity score matching (continued)

Population with Mood Disorder

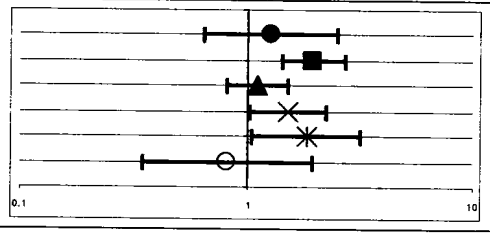
REF: Topiramate	RR [95% CI]	Sample Sizes*
Carbamazepine	1.28 [0.65-2.53]	17/763; 16/921
Gabapentin	2.00 [1.43-2.79]	95/5162; 55/5962
Lamotrigine	1.12 [0.81-1.54]	88/3405; 66/2872
Oxcarbazepine	1.46 [0.98-2.18]	61/1431; 40/1373
Tiagabine	1.83 [1.06-3.17]	35/954; 20/998
Valproate	0.90 [0.37-2.17]	9/386; 11/424

Attempted or Completed Suicide



REF: Topiramate	RR [95% CI]	Sample Sizes*
Carbamazepine	1.28 [0.65-2.53]	17/763; 16/921
Gabapentin	1.97 [1.42-2.72]	99/5162;58/5962
Lamotrigine	1.12 [0.82-1.53]	90/3405;68/2872
Oxcarbazepine	1.51 [1.02-2.24]	63/1431;40/1373
Tiagabine	1.83 [1.06-3.17]	35/954; 20/998
Valproate	0.82 [0.35-1.95]	9/386; 12/424

Attempted or Completed Suicide or Violent Death



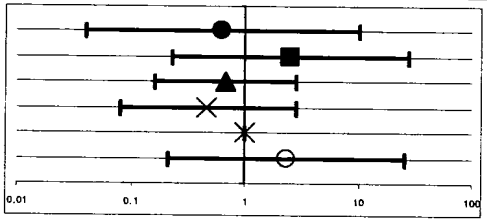
Carbamazepine
Gabapentin
Lamotrigine
Oxcarbazepine
Tiagabine
Valproate

*Drug events/PY; Reference drug events/PY

Population with Epilepsy or Seizure disorders

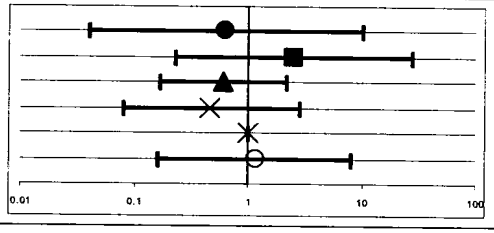
REF: Topiramate	RR [95% CI]	Sample Sizes*
Carbamazepine	0.64 [0.04-10.23]	1/271; 1/173
Gabapentin	2.52 [0.23-27.79]	2/147; 1/186
Lamotrigine	0.67 [0.16-2.80]	5/308; 3/123
Oxcarbazepine	0.47 [0.08-2.81]	2/246; 3/174
Tiagabine	-	0/22; 0/26
Valproate	2.30 [0.21;25.37]	2/46; 1/52

Attempted or Completed Suicide



Carbamazepine	0.64 [0.04-10.23]	1/271; 1/173
Gabapentin	2.52 [0.23-27.79]	2/147; 1/186
Lamotrigine	0.60 [0.17-2.13]	6/308; 4/123
Oxcarbazepine	0.47 [0.08-2.81]	2/246; 3/174
Tiagabine	-	0/22; 0/26
Valproate	1.15 [0.16;8.16]	2/46; 2/52

Attempted or Completed Suicide or Violent Death



Carbamazepine
Gabapentin
Lamotrigine
Oxcarbazepine
Tiagabine
Valproate

*Drug events/PY; Reference drug events/PY

** As treated analysis censoring at termination of health plan eligibility, treatment discontinuation, switching , event, or at 180 days whichever comes first